25 Haemoglobin Disorders n=88

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Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion
APPG	All Party Parliamentary Group
CMV	Cytomegalovirus
DHTR	Delayed haemolytic transfusion reaction
ED	Emergency department
FAHR	Febrile, allergic and hypotensive reaction
G&S	Group and screen
Hb	Haemoglobin
HCP	Healthcare professional
HSCT	Haematopoietic stem cell transplant
HSSIB	Health Services Safety Investigations Body
HSE	Handling and storage error
HTR	Haemolytic transfusion reaction
IBCT	Incorrect blood component transfused
ICU	Intensive care unit
IVIg	Intravenous immunoglobulin
NHR	National Haemoglobinopathy Registry
NHSE	National Health Service England
NHSBT	NHS Blood and Transplant
NTDT	Non-transfusion dependant thalassaemia
RCI	Red Cell Immunohaematology
SaBTO	Advisory Committee on the Safety of Blood, Tissues and Organs
SCD	Sickle cell disease
SCTAPPG	All-Party Parliamentary Group on Sickle Cell and Thalassaemia
Sp-ICE	Specialist Services Integrated Clinical Environment
SRNM	Specific requirements not met
WCT	Wrong component transfused

Key SHOT messages

- 2023 saw the highest number of HTR and hyperhaemolysis in SCD, leading to 2 deaths
- Alloimmunisation and HTR are a significant risk of transfusion in haemoglobinopathy patients and in particular SCD. The importance of weighing up the risks and benefits of transfusion and the need to provide blood components that meet the requirements for these patients may not be appreciated by healthcare professionals without specific expertise

Recommendations

- Haematology teams must be involved in the management of haemoglobinopathy patients presenting to secondary care and be consulted regarding transfusion decisions
- It is important to gain a full transfusion history from the patient and inform the transfusion laboratory when patients present to an unfamiliar hospital. The national database (Sp-ICE or equivalent) should be checked, and the patient's base hospital transfusion laboratory asked for previous transfusion records
- All haemoglobinopathy patients should have a baseline extended red cell phenotype or genotype prior to transfusion (Trompeter, et al., 2020)

Action: Hospital transfusion teams, clinical teams looking after patients with haemoglobin disorders, laboratory management

Introduction

Red cell transfusion is a cornerstone of treatment of SCD and thalassaemia. Transfusions can be given both electively and as an emergency during physiological stress (Davis, et al., 2017).

The number of incidents reported to SHOT in this patient group has been steadily increasing year-on-year. This year has seen the highest number yet, with 88 cases in total. There were 25 cases of major morbidity and 2 transfusion-related deaths reported. Figure 25.1 shows cumulative data for adverse transfusion events in patients with haemoglobin disorders since 2010 when SHOT started collating these reports.

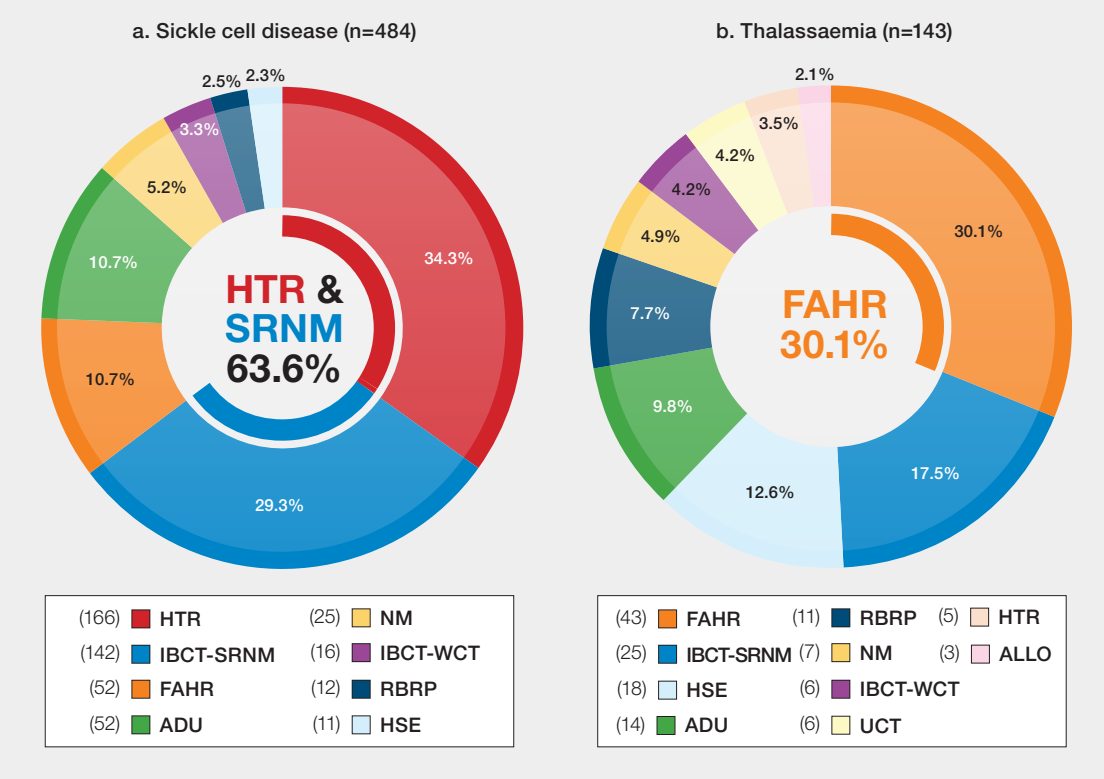


Figure 25.1: Cumulative data for adverse transfusion events in patients with haemoglobin disorders 2010 to 2023
a. Sickle cell disease (n=484)
b. Thalassaemia (n=143)

ADU=avoidable, delayed or under or overtransfusion; ALLO=alloimmunisation; FAHR=febrile, allergic or hypotensive reactions; HTR=haemolytic transfusion reactions; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; IBCT-WCT=IBCT-wrong component transfused; NM=near miss; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; TTI=transfusion-transmitted infection; UCT=uncommon complications of transfusion

Categories with 2 or fewer reports are not included in the figures

Deaths related to transfusion n=2

There were 2 deaths related to transfusion (imputability 2, probable) reported in 2023 in haemoglobinopathy patients. Both were patients with SCD that died from haemolytic complications following elective transfusions (one had hyperhaemolysis, one had a DHTR). Further details can be found in Chapter 19, Haemolytic Transfusion Reactions (HTR).

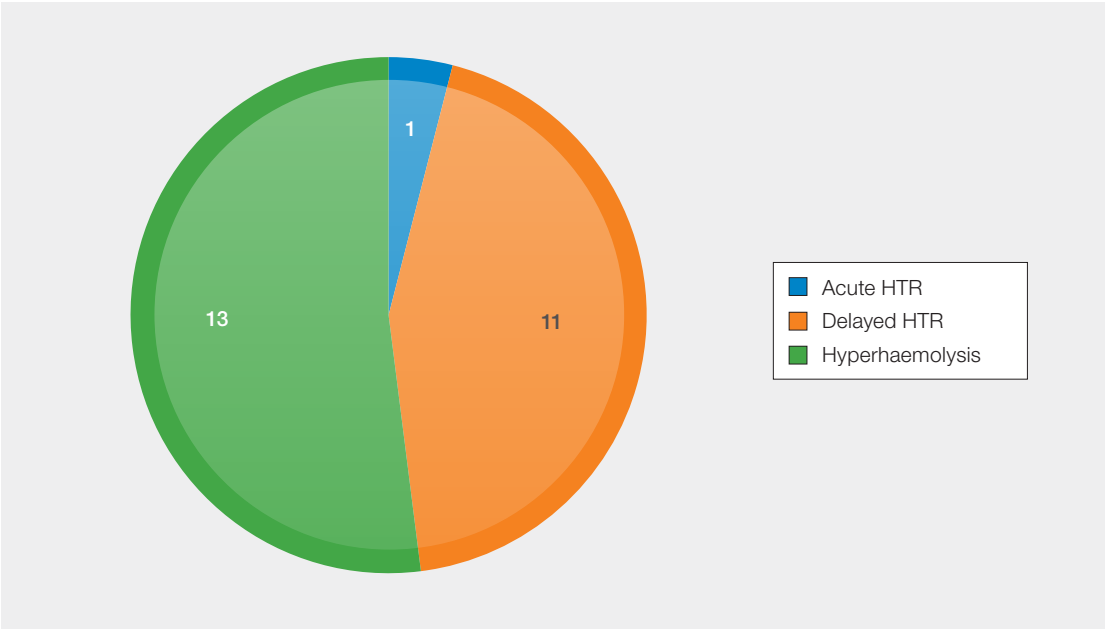
Major morbidity n=25

There were 25 reports associated with major morbidity, including 16 HTR, 6 FAHR, 2 delayed transfusions and 1 TTI.

Haemolytic transfusion reactions n=25

There were 25 reports of HTR in haemoglobinopathy patients, all in the context of SCD. This included 13 reports of hyperhaemolysis.

Figure 25.2: Types of HTR reported in patients with haemoglobin disorders in 2023 (n=25)



HTR=haemolytic transfusion reactions

Case 25.1: DHTR despite best practice

A patient with SCD sustained an ankle fracture and required surgery. They were known to have anti-S and anti-M antibodies. They received two compatible red cell units preoperatively and were discharged with appropriate safety-netting. The patient presented the following week to ED with sickle pain and anaemia. Their blood results showed evidence of significant haemolysis and they were treated with IVIg, steroids, rituximab and eculizumab. The patient received one unit of red cells during this treatment when her Hb dropped to 35g/L and spent 2 days on ICU before making a full recovery.

Case 25.2: Hyperhaemolysis recurrence after miscommunication

A patient with SCD presented to the ED with pain. It was noted that they had a Hb of 49g/L (baseline 50-55g/L). One unit of red cells was transfused overnight, after discussion with the on-call consultant haematologist. The next day, the haematologist noted that the patient had a history of hyperhaemolysis which had not been relayed on the phone overnight. The patient was subsequently started on steroids and was monitored as an inpatient for 2 days. They returned 3 days after discharge with pain and evidence of haemolysis. The patient remained in the hospital for 6 weeks, including 5 days on ICU.

Case 25.3: The importance of informed consent

A patient with SCD was admitted with a painful crisis. Two units of red cells were transfused, despite the Hb being at baseline for this patient. The indication for this transfusion was not clear. Six days later, they had an acute deterioration with hyperhaemolysis. The patient was admitted to ICU for 7 days, treated with IVIg, steroids and tocilizumab and subsequently made a full recovery. On discharge, the patient expressed concern that the rationale for the initial transfusion was not explained to them. There was no documentation of consent for the transfusion.

Another case involving DHTR and death after an exchange transfusion has been described in detail in Chapter 19, Haemolytic Transfusion Reactions (HTR), Case 19.1. It demonstrates the importance of communication and coordination between medical teams in this complex patient group.

Learning points

- Hyperhaemolysis is a serious complication of transfusion in SCD patients and can lead to death and serious morbidity. It can occur despite giving extended phenotype-matched red cells and without laboratory evidence of new alloimmunisation. Alloimmunisation and HTR can have serious implications on future transfusion provision in a cohort who may often need transfusion across their lifespan. Patients should be fully informed about the specific risks of alloimmunisation and HTR during the consent process, and unnecessary transfusions must be avoided
- Timely and effective communication between clinical and laboratory staff, between hospitals and between teams is vital for safe transfusions
- Patient education and understanding of the reasoning behind interventions is fundamental to ensure safety. This may empower them to challenge when things are incorrect. Staff should also question and check whether interventions are required
- A detailed and accurate transfusion history is essential, particularly when patients present to a new hospital

Febrile, allergic and hypotensive reactions n=13

There were 13 reports of FAHR, 7 of which were in patients with SCD, and 6 occurred in patients with thalassaemia. All patients made a full recovery.

IBCT-specific requirements not met n=16

There were 16 cases of SRNM.

Case 25.4: Avoidable alloimmunisation in a patient with thalassaemia

A patient with NTDT required a red cell transfusion during pregnancy. The laboratory was not informed that the patient had thalassaemia on the first 'booking' G&S, so Rh and K typing were not performed. The second G&S sample did include the relevant clinical information, but the required testing was not performed. Three red cell units were issued to the patient without being Rh/K-matched. The patient made an anti-c and anti-E antibody as a result.

Case 25.5: SRNM in SCD

A patient with SCD presented to hospital with a Hb of 49g/L. The LIMS had a flag to say that the patient had SCD, but this was not noted. Rh and K typing were not performed. The patient was O D-positive, but O D-negative red cells were provided for stock management reasons, though the transfusion was not an emergency. No pre-administration checklist was in use in the hospital, so specific requirements were not checked at the bedside. The case was picked up on a subsequent audit of O D-negative red cell use.

Case 25.6: Confusion about red cell matching post HSCT

A patient with SCD required a red cell transfusion after an allograft. Laboratory staff were unclear whether the Rh phenotype would be maintained post transplant, and this was not made clear on the local protocol. This has since been clarified and the post-HSCT protocol updated.

There were 3 reported cases of CMV-unselected red cells being given to pregnant haemoglobinopathy patients on regular transfusion programmes in 2023.

Learning points

- Laboratory staff must be informed when patients have a haemoglobinopathy, particularly when patients are new to a hospital. This will help ensure specific transfusion requirements are met and previous alloimmunisation is not overlooked for this patient cohort
- There may be additional specific transfusion requirements for some patients which must be taken into consideration when issuing blood components, e.g., irradiation post HSCT or CMV-negative components when pregnant (SaBTO, 2012)
- As HSCT for haemoglobinopathy patients becomes more common, protocols for blood provision need to be updated
- A joint statement from NHS Blood and Transplant, National Blood Transfusion Committee, United Kingdom Thalassaemia Society and Sickle Cell Society issued in November 2023 confirms removal of maximum age requirements for red cells transfusion to patients, including those with haemoglobinopathies, and can be accessed at this link: nhsbt-removal-of-maximum-age-requirements-for-red-cells-transfusion-to-patients-including-those-with-haemoglobinopathies.pdf (b-s-h.org.uk). It has been agreed that the BSH guidelines on red cell transfusion in sickle cell disease and on pre-transfusion compatibility procedures in blood transfusion laboratories will be updated in this respect. The SRNM definition and reporting criterial will also be updated in due course to reflect these changes

IBCT-wrong component transfused n=4

There were no reports of ABO-incompatible blood transfusions in patients with haemoglobin disorders in 2023.

Avoidable, delayed or under/overtransfusion n=12

There were 12 cases of avoidable or delayed transfusions, of which 2 led to major morbidity.

Case 25.7: Delayed exchange transfusion

A teenage patient with SCD required an emergency exchange transfusion due to acute chest syndrome. The patient had a new positive antibody screen. The blood had been sent in a paediatric tube, so there was insufficient serum for RCI testing. Two further samples were sent, but one sample tube had expired and the other was both insufficient and incorrectly labelled. Further samples then had to be collected. In the end, provision of appropriate red cell units took 22 hours.

Learning points

- Acute chest syndrome can result in rapid deterioration and respiratory failure. Multiple guidelines and consensus statements support the use of early transfusion in this condition (Howard, et al., 2015)
- Effective inventory management should be in place to avoid using expired sample tubes. Reminders for upcoming expiry dates, clear labelling and minimising overstocking can mitigate the risk of using expired items

Handling and storage errors n=8

There were 8 cases of handling and storage errors when transfusing patients with haemoglobinopathies in 2023. Most of these involved issues with infusion pump settings including staff being unfamiliar with equipment. None of these incidents led to major morbidity.

Transfusion-transmitted infections n=1

There was 1 confirmed case of transfusion-transmitted malaria in a young child with thalassaemia in 2023. This is described in Chapter 21, Transfusion-Transmitted Infections (TTI), Case 21.5.

NHR-NHSBT data linkage

The National Haemoglobinopathy Registry (NHR) is a register of people in the UK with all types of inherited red cell disorders. The register is held by NHSE and is intended to support direct clinical care, and for commissioning services within England. The NHR-NHSBT data linkage went live on Tuesday 12th March 2024. NHSBT red cell antibody data held on NHSBT systems is now available in the NHR on the transfusion tab and will be clearly marked as NHSBT red cell antibody records. This is a significant improvement in transfusion safety for patients who may need blood transfusion either as part of routine care or as an emergency. The data transfer will happen routinely every night to ensure new results move into the NHR, so the data is as up to date as possible.

This is a key milestone for NHSBT and NHSE in ensuring that critical results important for safe transfusion practice are available to clinical teams who need the information. All hospitals will continue to communicate with the patient's normal haemoglobinopathy centre transfusion laboratory to ensure that any results that may not be part of the NHSBT antibody record are also included in any decision-making regarding transfusion.

Conclusion

This year saw the highest number of SHOT reports in patients with haemoglobinopathies. Most major morbidity came from HTR, particularly hyperhaemolysis. Patients must be adequately informed and consented for these risks when a transfusion decision is being considered. This should be clearly documented in the patient's notes in line with SaBTO guidance. Consent should be reviewed frequently for those on regular transfusion treatment (SaBTO, 2020).

To reduce the risk of HTR and alloimmunisation, all haemoglobinopathy patients are eligible for full red cell genotyping as part of the 'Haem Match' project, which should help to more accurately match appropriate donors to patients (Gleadall, et al., 2020).

A common theme in the case studies above is the lack of adequate communication. Effective communication between hospitals, within hospital teams and between clinicians and the laboratory is vital to ensure that transfusion errors do not occur. In addition, good communication with patients to explain interventions and to take a thorough transfusion history is also crucial, particularly when patients present to unfamiliar hospitals. The antibody history for haemoglobinopathy patients is available to laboratory staff on Sp-ICE or other similar national databases. This has recently been added to the NHR.

The lack of experience in managing SCD patients in areas outside of haematology was highlighted in the APPG 'No One's Listening' report (SCTAPPG, 2021). The HSSIB recommended that NHS England review whether there should be a minimum training requirement for all HCP about SCD after an investigation in 2023 (HSSIB, 2023). The case studies above demonstrate that this is an ongoing problem. The message that haemoglobinopathy patients outside of haematology wards should have haematologists closely involved in their care and their transfusion decisions needs emphasising further.

A recent Lancet article summarised strategies to improve outcomes for SCD patients worldwide (Piel, et al., 2023). Transfusion availability and safety were key aspects of this. While the UK has a relatively robust and safe blood supply, as demonstrated above, improvements must be made to enhance transfusion safety for this patient group.

Recommended resources

SHOT Bite No. 14: Transfusion errors and reactions in patients with Haemoglobinopathies
SHOT Bite No. 15: Hyperhaemolysis
https://www.shotuk.org/resources/current-resources/shot-bites/

SHOT Video: Haemolytic Transfusion Reactions in patients with Haemoglobinopathies
https://www.shotuk.org/resources/current-resources/videos/

SHOT Safety Notice 02: SRNM 2022
https://www.shotuk.org/resources/current-resources/safety-notices/

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