BSH 2020 VIRTUAL
9 -14 NOVEMBER
British Society for Haematology
Listening • Learning • Leading
BSH2020-771

Alloimmunisation in Sickle Cell Disease in the North Central London Haemoglobinopathy Cohort: providing a baseline for extended red cell antigen matching and targeted donor genotyping

K Fordwor*[1], A Pain*[2], K Madgwick[3], N Gleadall[4], S Trompeter[5,6], S Stanworth[1,7], E Aimiuwu[8], E Prescott[9], S Marston[9], I Longair[10], N Malone-Cooke[9], O Wilkey[11], A de Kreuk[3,5], E Drasar[5,9], F Shah[5,9], P Eleftheriou[5], J Porter[5,], D Roberts[1,7], W Ouwehand[6,12], F Regan[6,13].

[1]Haematology, Oxford University Hospitals NHS Foundation Trust, Oxford, [2] Medicine, Buckinghamshire Healthcare NHS Trust, Buckinghamshire , [3]Haematology, North Middlesex University Hospital NHS Trust, London, [4] Haematology, Addenbrook's Hospital, Cambridge, [5] Haematology, University College Hospitals NHS Foundation Trust, [6] Haematology, NHS Blood and Transplant, London, [7] Haematology, NHS Blood and Transplant, Oxford, [8] Paediatrics, [9] Haematology, Whittington Health, [10]Blood Transfusion, Health Services Laboratory, [11] Paediatrics, North Middlesex University Hospital NHS Trust, [12]School of Clinical Medicine, University of Cambridge, Cambridge, [13]Haematology, Imperial College Healthcare NHS Trust, London

INTRODUCTION

In the UK there are approximately 14,000 patients with sickle cell disease (SCD)[1]. For a significant number of these patients, their medical lives are defined by access to, need for and complications of blood transfusion. This has become ever more true as the role of transfusion has expanded in sickle care. Alloimmunisation through transfusion remains one well-recognised complication in this population. As a result the patient is at an increased risk of delayed transfusion reactions or hyperhaemolysis which can be life-threatening[2]. The sourcing of blood for those with certain types or combinations of alloantibodies as an emergency or as part of a long- term transfusion programme is also a well-recognised challenge in this setting and can be complicated and laborious. In some cases, sufficient numbers of typed units may not be available rendering the patient 'un-transfusable'. The rate of alloimmunisation in SCD patients has been estimated to be between 7 and 47 percent[3]. There are patient specific factors that may increase a patient's susceptibility to developing alloantibodies, including the presence of particular HLA alleles and reduced peripheral CD4+ regulatory T cell suppressive function[2]. The chronic inflammatory state caused by SCD may also play a role[2]. In spite of these factors, the major cause in the development of alloimmunisation is thought to be the mismatch of donor and recipient red cell antigens due the difference in ethnic origin. The majority of the patients with SCD are of African ethnic origin, however, in the UK and other Western countries that vast majority of blood donors are of European descent. In the UK extended matching for ABO, Rh CcDEe and Kell is now standard practice when transfusing all SCD patients, which in theory should help. There are some that would argue that extended matching beyond this would be desirable[4], yet the feasibility and choice of which antigens to match against has yet to be determined[5]. The use of phenotyping to match blood (which is standard of practice) still results in high levels of alloimmunisation in patients[6]. As a result there has been an increasing move towards genotyping SCD patients instead, in order to better characterise their red cell antigen profiles and identify variants that previously may not have been detected.

AIM

The aim of this project was to document and characterise the numbers and patterns of red cell antigens and alloantibodies in a large current cohort of patients with haemoglobinopathies. We also aimed to determine which and to what extent extended matching practices are currently employed in North London.

METHOD

Transfusion data was collected on 2028 haemoglobinopathy patients across the North Central London Sickle Cell and Thalassaemia Network (NCLSTN), linking UCLH, Whittington Health and North Middlesex Hospital. Patients were identified from local databases, the National Haemoglobinopathy Registry and Blood Transfusion Laboratory Information Management Systems (LIMS). Patients identified with their main treating centre elsewhere at the time of data collection were excluded. Antibody and antigen status was identified from the Blood Transfusion LIMS, as well as NHSBT SpICE. Demographic and treatment plan data was collected using hospital records. The data was pseudo-anonymised on an excel spreadsheet and analysed using SPSS. The researcher had an honorary contract at all three sites.

RESULTS

In our population, 1334 patients had SCD (66%) (Figure 1). Of the 1334 patients, 976 had HbSS (73%), 316 were <18 years old (24%) and 199 were on a regular transfusion programme (15%) (Figure 2).

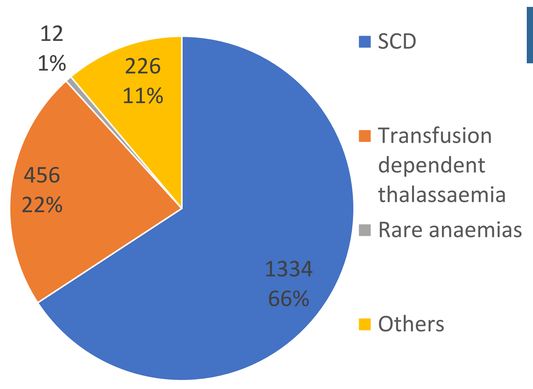

Figure 1: The haemoglobinopathy diagnoses in our population

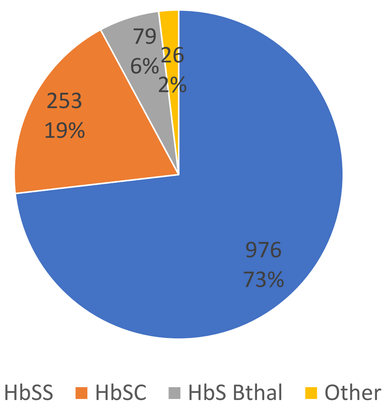

Figure 2: The frequency of specific haemoglobin diagnoses in our sickle cell population

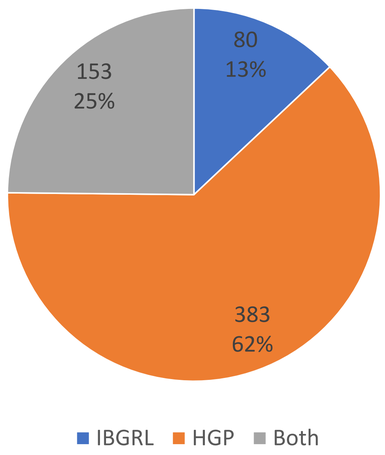

Figure 5: The proportion of patients in our sickle cell population with genotype analysis

262 patients with SCD (20%) had alloantibodies and/or autoantibodies; of these, 81 were on regular transfusions (Figure 3). Anti S was the most common alloantibody 42/1334 (3.1%), then Anti E 39/1334 (2.9%), Anti Kpa 30/1334 (2.2%), Anti K 28/1334 (2.1%), Anti C 27/1334 (2.0%), Anti M 21/1334 (1.6%), Anti Cw 20/1334 (1.5%) (Figure 4). Only 616 of the 1334 patients (46%) with SCD had a genotype performed with variant analysis (Figure 5). In this group, Blood Group O 293/616 (48%), C variants 51/616 (8.3%), Rh variant 119/616 (3.1%), U negative or variant 19/616 (3%).

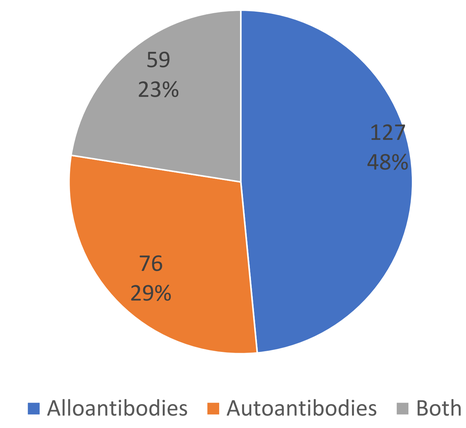

Figure 3: The frequency of alloimmunisation and autoimmunisation in our sickle cell population

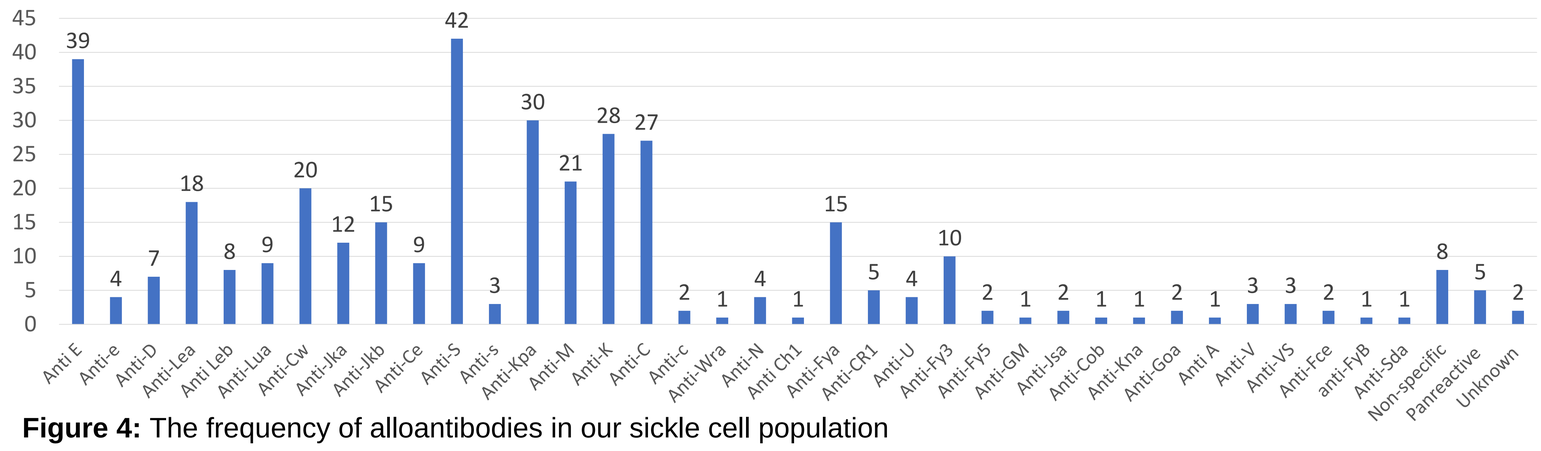

Figure 4: The frequency of alloantibodies in our sickle cell population

CONCLUSIONS

Analysis of this cohort of SCD patients has shown an alloimmunisation incidence of 14% which correlates with previously reported estimates. The majority of these instances relate to sensitisation to Rh and Kell antigens, which is previously well documented[3]. Previous studies suggest this is most likely caused by the presence of Rh variants in patients and donors that may not be detected by phenotyping[7]. Most Rh alloimmunisation we found is likely to be historical or has occurred when the the blood bank at a hospital new to the patient is unaware of their sickle status. The rates of alloimmunisation to M and S antigens are also high, and may reflect that previously, matching for these antigens was not a priority. Unsurprisingly, higher rates of alloimmunisation were seen in those on regular transfusion programmes. It is important to note however, that the majority of regularly transfused patients failed to develop any alloantibodies despite regular exposure to non-extended matched blood products.

The analysis of this large cohort also highlights the issue faced by U negative or variant patients, which in North London total 3% of the cohort. In the general population the prevalence of those with this phenotype is much lower, making it often exceedingly difficult to source enough units to exchange these patients, particularly with short notice as may be required in an acute sickle crisis. If a patient additionally has an alloantibody this can make it almost impossible to transfuse the patient.

The most worrying aspect of this data is that 24% of the alloimmunised patients are under the age of 18 and many of these patient are likely to require transfusion for various indications in the future. It is accepted that patients who have developed one alloantibody are at greater risk of developing others[5], and in this group of young patients this could result in them becoming progressively difficult to transfuse over the course of their lifetime. It is also important to highlight that many of these young patients will have developed alloantibodies despite the use of extended phenotyping and matching.

Our findings support the need to better understand the national burden of alloimmunisation in haemoglobinopathies and the impact on patient care, but also to explore new strategies for optimising matching and timely delivery of blood as proposed by the HAEM-MATCH consortium. Further work is planned to add to this cohort so that we can ascertain risk of alloimmunisation and with donor genotyping develop a matching strategy for a precision transfusion model algorithm and a pilot study of better matched blood. One approach is the application of new technologies for cost-efficient genotyping, which might support a reconfiguration of the entire process of blood grouping, matching and selection of blood, Furthermore, by identifying the optimal antigen profiles for our patient cohort, the donor recruitment strategy can be refined and donors could be targeted for donations with precision.

REFERENCES

1. Dormandy E et al. How many people have sickle cell disease in the UK? *J Public Health 2018; 1:40(3):e291 –e295*
2. Yazdanbakhsh K et al. Red blood cell alloimmunization in sickle cell disease: pathophysiology, risk factors, and transfusion management. *Blood 2012; 120(3): 528-537.*
3. Chou S et al. High prevalence of red blood cell alloimmunization in sickle cell disease despite transfusion from Rh-matched minority donors. *Blood 2013; 122 (6): 1062-1071.*
4. Compernolle V et al. International Collaboration for Transfusion Medicine Guidelines. Red blood cell specifications for patients with hemoglobinopathies: a systematic review and guideline. *Blood 2018; 58(6):1555-1566.*
5. Trompeter S et al. Position paper on International Collaboration for Transfusion Medicine (ICTM) Guideline 'Red blood cell specifications for patients with hemoglobinopathies: a systematic review and guideline'. *Br J Haematol 2020; 189(3):424-427.*
6. Trompeter S et al. The haemoglobinopathy survey: The reality of transfusion practice in sickle cell disease and thalassaemia in England. *Transfus Med 2020; doi: 10.1111/tme.12732. Online ahead of print.*
7. Chou S et al. RH genotype matching for transfusion support in sickle cell disease. *Blood 2018; 132 (11): 1198-1207.*

CONTACT INFORMATION

Dr Sara Trompeter

University College London Hospital NHS Foundation Trust, Haematology Department, 250 Euston Road, London NW1 2PG, UK.

Email: sara.trompeter@nhs.net

BSH2020
PO-189-A
Transfusion
Sara Trompeter
Poster presented at: British Society for Haematology Listening • Learning • Leading
PosterSessionOnline.com