



Article

TIF Standards for Haemoglobinopathy Reference Centres

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Abstract: Haemoglobin disorders are hereditary, lifelong and characterised by the need for multi-faceted management. The question of quality in meeting standards of care that are likely to bring the best possible outcomes for patients is a necessary consideration. The concept of reference centres supporting peripheral treatment centres in a formal networking relationship is a response to the real needs of patients and a practical solution in public health terms. In this report, a team of advisors of Thalassaemia International Federation (TIF) attempts to suggest a set of standards for haemoglobinopathy reference centres, also based on the founding principles of TIF, aiming to act as a guideline for its member associations and professional collaborators. The standards described herein can form the basis of an accreditation process and also serve as a guide for those who would advocate for quality improvement for thalassaemia services.

Keywords: thalassaemia; sickle cell disease; haemoglobinopathies; reference centres; standards of care



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1. Introduction

Haemoglobin disorders are hereditary and lifelong and, despite a wide spectrum of severity, are characterised by the need for multifaceted management. In the most severe form, death in infancy is inevitable without treatment. As described in evidence-based protocols [1,2], modern medicine has proven that prolonged survival and productive life are possible [3–5]. The recommended patient management consists of:

- Blood transfusions, which vary from very frequent to sustain life to occasional medical emergencies.
- Iron chelation, which aims to reduce iron that comes from increased absorption in the case of anaemia or the regular transfusions in the more severe forms.
- Constant monitoring of iron load and organ function, which is part of the routine of patient care
- Support from a multidisciplinary team of experts, especially in cardiology and endocrinology, which aims at proactive detection of organ damage and early, appropriate therapeutic response.
- Adherence to evidence-based guidelines and standards.
- Quality holistic care, which includes psychosocial support and quality of life promotion, allowing patients to approach “normality” in their daily lives.

Dedicated clinical service can reduce morbidity and prolonged survival, with an age distribution indicating a patient population nearing 50 years on average.

Epidemiological data and support from the central health administration are required to plan such a clinical service. Even in high prevalence areas, patients are often scattered in a geographical area, which does not always allow regular access to a centre of expertise with all the services described above. Knowing the number of patients will indicate the best location for expert assistance. Knowing the patient’s geographic location will help provide routine care (such as blood transfusion) near home while setting up a network between the peripheral and expert centres. This will ensure equity in the level of care

of all patients. Such planning requires recognition of the needs of patients from health authorities who can benefit from a registry. Epidemiological knowledge and especially spatial epidemiology, is basic for the better understanding of the real burden of disease and the initial step to recognising and planning to meet a need for care, which is a basic human right for any member of the population [6,7]. Epidemiology requires a system of diagnosis and recording of all cases.

Based on the need for experienced multidisciplinary collaborative medical care, treatment centres have developed in high-prevalence countries, concentrating on the appropriate services and providing day transfusion and outpatient clinics separate from other hospital services. Where patient numbers are low, clinical services are usually shared with other haematology patients, including malignant blood conditions. Where they exist, dedicated haemoglobinopathy centres are a model for the provision of complex care and become a second home for patients with chronic, lifelong needs for medical attention, in which patients and staff develop a unique relationship over time. Availability depends on adequate patient numbers to support such a service. Consideration is given to patients living far from the centre and how their needs are best served.

As for other healthcare services, the question of quality in meeting standards of care that are likely to bring the best possible outcomes for patients is a necessary consideration. Disease-specific specialised centres have not been singled out for quality assessment, with few exceptions such as haemophilia [8]. TIF has recognised the need for quality-assured or accredited reference centres for haemoglobin disorders as an umbrella organisation promoting patient interests worldwide.

The concept of reference centres supporting peripheral treatment centres in a formal networking relationship is a response to the real needs of patients and a practical solution in public health terms. Nearer to home, school, and work, patients may receive routine transfusions, medications, and investigations. During periodic visits to the reference centre, specialised tests and multidisciplinary consultations will determine changes in treatment and other interventions to be applied either at the reference centre or at the home centre. The frequency of visits to the reference centre may be routinely determined and/or according to individual needs [9].

This hub and spoke concept is not new in chronic care, especially for rare conditions. It is the basis of the European Reference Network system [10].

The complex needs of specialised care that haemoglobinopathy patients demand has prompted the Thalassaemia International Federation and its advisors to consider standards for disease-specific reference centres. The aim is to ensure the quality and completeness of services with favourable patient outcomes as the final objective. Any treatment unit used by thalassaemia and sickle cell patients, including day transfusion and out-patient clinics, must satisfy certain principles:

- The first is a concern for patient safety;
- The addition of adherence to standards of care;
- Good patient communication;
- Keeping good medical records;
- Adequate and qualified professional staffing;
- Continuity of care;
- A holistic patient-centred approach, with the patient partnership.

These are all principles often taken for granted and just as often put aside. Satisfying such principles requires a governance structure with a vision and a budget to adequately support the service and maintain the required standards.

In this report, a team of advisors attempts to suggest a set of standards for haemoglobinopathy reference centres, also based on the founding principles of the Thalassaemia International Federation, aiming to act as a guideline for its member associations and professional collaborators. It aims to be a guide for those who would advocate for quality improvement for thalassaemia services.

2. Methodology

Preliminary work was initiated with a questionnaire distributed to treatment centres worldwide, aiming to identify the services offered and the degree of recognition as reference centres through accreditation by international agencies, academic bodies, or health authorities. This survey was conducted before the COVID-19 pandemic.

3. Results

3.1. Survey Response

A survey was sent to 142 centres treating haemoglobin disorders, including alpha and beta thalassaemias and sickle cell syndromes. A total of 86 (60.6%) centres were from high-income countries (World Bank listings 2021), 34 (23.9%) from upper-middle-income countries, and 22 (15.5%) from low-middle-income countries.

Of the respondents, 12 stated that they did not directly treat patients (mainly in laboratories). Of the 130 remaining, 27 dealt with less than 50 patients of all categories, while 103 treated more than 50 patients and could be regarded as reference centres based only on numbers.

3.2. Assessment of the Level of Services

We isolated the following indices to assess the level of services:

- (1) Accreditation: Centres were asked whether they had any kind of accreditation as reference centres. There were 116 responses, of which 20 have an international award (JCI, JCIE, ISO, and one is a WHO Collaborating Centre); 14/20 from high-income countries, 4/20 from upper-middle-income countries, and 2 from lower-middle-income countries. Another 37 claim a national recognition or accreditation, 59 have no recognition, and another 14 did not respond. Overall, 15.4% (20/130) of treatment centres were awarded an internationally accepted accreditation.
- (2) Patient registers: Of 130 treatment centres, 88 (67.7%) have a local register (mostly paper or Excel), 26 (20%) are connected to a national registry, while 16 (12.3%) have no register.
- (3) MRI to measure tissue iron: A total of 123/130 (94.6%) claim to perform annual cardiac T2* iron measurements, and 58/130 (44.6%) are also connected to FerriScan for R2 LIC measurements. Only 7 centres stated no MRI available.
- (4) Specialist monitoring: A total of 125 centres stated annual cardiology examinations for their patient, and 126 centres stated regular endocrinology examinations.
- (5) Availability of iron chelating agents: A total of 106/130 (81.5%) had all three iron chelators, and 21 (16.1%) did not have deferoxamine. This includes some high-income countries, where it is presumed that regulatory authorities had not approved this medicament. In addition, isolated centres stated nonavailability in countries where other centres had all three drugs; one example was a centre in Greece that stated only deferoxamine was being offered in contrast to all other centres from that country.
- (6) Transcutaneous O₂ saturation: The vast majority of centres with a sizeable number of sickle cell patients have this service available within the centre, though 19 centres did not have this available, even though the SCD patients ranged from 10 to 550. This is a quality indicator, but the 19 centres were not related to the number of patients or the development of the country where they are located.
- (7) Use of evidence-based clinical management guidelines: A total of 128 centres responded to this question. A total of 67 (52.3%) used guidelines for SCD and thalassaemia, 45 (35.2%) used guidelines for thalassaemia only, while 7 (5.5%) had guidelines only for the management of sickle cell syndromes (6 of these centres are in countries where SCD is a rare immigrant condition), and 9 (7%) centres did not follow any specific guidelines—6 of these were in countries where thalassaemia is a rare condition, mainly affecting the migrant population. It should also be noted that 12 of the 45 centres that use only thalassaemia guidelines (26.7%) follow a significant number of SCD patients (20-450) and should have both guidelines available. Of the seven

centres that stated they follow only SCD guidelines, only one also had large numbers of thalassaemia patients (190).

- (8) Free of charge services: From 129 responses, completely free (with no out-of-pocket expenses) was stated by 98 (76%) of centres, while in 27 centres (20.9%), there is partial coverage. In four centres (3.1%), services were exclusively out of pocket.
- (9) Involvement in research: Only 23 (17.7%) from 130 treatment centres admitted not being involved in research. The rest presented subjects that have led to research and publications concerning various topics concerning haemoglobin disorders.
- (10) Professional psychosocial support: A total of 93 of 129 (72%) centres stated that they offered a service from experienced staff within the centre. In contrast, the rest, 36 (28%), either did not provide support or refer patients to agencies outside the centre. Nevertheless, most centres are catering for monitoring and multidisciplinary care.

3.3. Quality of Care Analysis

Ten criteria were used to assess the quality of care. These self-reported results may include an element of bias, and TIF local visits confirm this. The fact that only 20 centres have achieved or even sought accreditation indicates a possible assumption that all is well or a lack of interest in quality improvement. It must also be noted that these responses reflect a snapshot of the centres' impressions when responding to the inquiry. Most centres recognise the multiorgan involvement in haemoglobin disorders and seem to provide proactive monitoring. However, about 20% of centres did not have all three chelating agents, which casts doubt on their ability to tailor iron load management to individual patients' needs and their claim to be reference centres. It was observed that national regulatory authorities in some countries had not licenced deferiprone. However, an expert clinician has to demand the availability of all tools that will give the patients the greatest chance to minimise complications). Overall, only 73 (56%) of these 130 reference centres seem to have good clinical practice guidelines for all the patients they treat. The relatively limited use of evidence-based guidelines, and especially the fact that almost a quarter of services are not completely out of pocket for such lifelong disorders, are indicators that cause doubt also regarding the quality of care.

Almost half of the responding centres had sought recognition as centres of expertise or as reference centres. Only the 20 that had sought to satisfy international quality standards for accreditation can be said to have objective evidence of having reached such high standards. In addition, these are general standards, and TIF advocates for creating disease-specific centres of excellence, able to offer the kind of comprehensive services that can achieve the desired outcomes of prolonged survival and good quality of life. Good clinical practice guided by the standards suggested by the various internationally recognised bodies mentioned above prompted our team to propose a model for thalassaemia services. A preponderance of responses from centres located in high-income countries reflected the variable quality of services. It is essential to emphasize that 80% of the patient population lives in low-middle-income countries, more often in peripheral hospitals and even primary care settings. The lack of equity in patient care is well recognised; sub-standard management is the rule and not the exception, and out-of-pocket expenses for families in the low-income bracket are very common [11].

These observations led to a team of experts suggesting the standards for reference centres. These suggestions were based not only on their experience in the management of haemoglobin disorders, but also through an extensive literature review of standards such as EUCERD criteria [12], standards set for the European Reference Networks [13], the Chronic Care Model [14], ISQua guidelines [15], the American Institute for Healthcare Quality AIHQ, quality standards set by the UK Forum on Haemoglobin Disorders [16], and the Joint Commission International Accreditation Standards for Ambulatory Care [17].

3.4. TIF Suggestions for Thalassaemia Reference Centres

The following principles were put forward by the expert group based largely on JCI-suggested principles [17]:

(1) Governance

- A hierarchical structure should include a chief executive/managing director and a coordinated, professional team that includes multidisciplinary services, recognising the complex pathology of haemoglobin disorders.
- The administrative structure and staff organisation should clearly describe the rules and regulations of the centre's services.
- A clear definition of the centre's mission and the existence of policies and programmes to fulfil the mission.
- Ensuring staff qualifications, experience, and continual education. Staff qualifications, skills, knowledge, and experience are defined and described along with the job description.
- Staff includes the specialist practitioners who may serve the patient's needs even if their regular position is outside the centre.
- The staff's expertise in haemoglobin disorders assessment and management must be assured.
- The centre's leadership should ensure good communication between the centre's staff, the specialist contributors, and services such as the blood bank.
- The management monitors and evaluates the centre's functions, including staff performance and patient safety. This includes a clinical audit aiming to assess if the facility is attaining the recognised standards [18].
- The advocacy for quality improvement and continued development according to scientific advances (including innovative therapies) to health authorities [19].
- Connection with patient support associations, with patient representation on advisory bodies.
- All stakeholders' views regarding matters of priority and focus on any quality improvement activity are taken into account.
- All decisions are based on data, obtained through patient records and outcomes and any new developments noted through publications and trials.
- The governance of patient data is an administrative responsibility.
- A culture promoting ethical practices in all aspects of administration and clinical care should be ensured, considering internationally accepted patients' rights.
- The administration is responsible for overseeing and ensuring that internationally accepted principles guide any research involving patients or patient-derived data and that expert ethical approval and patient consent have been obtained. Clinical research is an additional indicator of good clinical practice if regulated and aimed at benefitting patients.
- It is the responsibility of management and senior staff to seek accreditation according to international standards. This is not a frequent objective, but the long-term benefits to patients are well-supported [20].

(2) Safety concerns

- Staff education on safety is programmed. This includes both staff and patient safety.
- Patient identification is clear in individual records (electronic or paper-based), blood transfusions, and lab results
- There is effective patient communication and explanation of all interventions.
- Haemovigilance [21] and pharmacovigilance are practised, including drug safety alerts.
- There are evidence-based hand hygiene guidelines.
- Methods and procedures to minimise the risk of infection within the treatment centre are in place. A practical example in recent times is the prevention of

COVID-19 transmission in patients arriving for preparation and to receive blood transfusions or visit their doctor [22].

- The danger of transmitting blood-borne infections, especially hepatitis viruses, is a priority. There is constant communication with the blood bank, including knowledge of the safety practices in donor selection. Monitoring both by serological methods and molecular methods is implemented according to international recommendations for regularly transfused patients.
- There are measures to reduce accidents, such as falls in the centre. A secure environment is planned and regularly inspected. Hazardous material handling and disposal (such as needles) are part of the centre's daily procedures.
- There are treatment rooms and resuscitation equipment.
- Fire safety and certification by the country's fire services are available. This includes regular testing of any devices required for fire control.
- Cigarette and other smoking is forbidden on the premises.
- Emergency procedures are in place in the event of power and water cuts or contamination. Monitoring of water quality is performed regularly.

(3) Access to care

- The centre clearly serves benign haematology patients and does include malignancies as they constitute a dangerous and vulnerable cohabiter.
- Patient flow: there must be adequate numbers of patients in each diagnostic group—at least 50 thalassaemia patients and/or 50 SCD patients for the centre to be regarded as experienced.
- Continuity of care is safeguarded by low staff turnover and the presence of experienced and qualified caregivers.
- Clinical records with lifetime data are kept.
- Multidisciplinary care is provided with a referral system where necessary and collaboration with in-patient services [1,23].
- Networking the reference centre with secondary and other centres of excellence nationally or internationally is an added value.
- A twinning programme with an academic centre is also an additional advantage.
- Any existing electronic health record must fulfil all the patient safety requirements, including patient consent, confidentiality, and anonymisation in data storage and sharing of data for research.
- Barriers to patient access, including distance, language, cultural or religious barriers, are considered and appropriately addressed.

(4) Partnership model

- Adequate information is always provided to patients/families about the disease and any treatment decisions, including possible side effects. Patient education is a prerequisite to partnership and shared decisions [24].
- Good communication is the basis of the doctor–patient relationship.
- Patients are given choices about their treatment.
- Self-management is encouraged, particularly in haemoglobin disorders, in which daily home treatment is the basis for preventing complications and survival. The patient must be aware of possible complications of the condition and its treatment and know when to inform the care team when warning signs and symptoms appear.
- Special attention to patient adherence is given, and the patients are supported appropriately.
- Workshops for patients/families are held regularly, at least once a year, in a language that laypersons can understand.
- Respect for patient rights and time is a must in all cases. This includes personal values and beliefs as well as privacy and confidentiality.
- Informed consent for all procedures is obtained. This includes the use of blood.

- (5) Guidelines and standards for clinical care
 - Evidence-based national guidelines put together by experts in the field or international guidelines (e.g., TIF) are used in the centre and adhered to.
 - Guidelines and standards include diagnosis and monitoring as well as medical treatment.
 - Lifestyle advice, nutritional needs, and psychosocial needs are subjects requiring standards, advice, and support [1,25,26].
 - Pain screening is performed and a pain management system is in place. Pain, both chronic and acute episodes, is common in patients with haemoglobin disorders [27].
 - Investigation of the underlying cause as well as management are basic requirements.
 - Assessing the quality of laboratory and other technologies used to monitor patients is the responsibility of the clinical team, which must alert the providers of any divergent or inaccurate results. One example is the accuracy of MRI iron measurements for which instruments' calibration and validation are required.
 - Infection control procedures are part of the clinical standards of the centre.
 - Availability of food during day care is necessary. The quality and nutritional value must be monitored.
 - Blood transfusion procedures and standards according to international directives are kept [21].
 - Any medical treatment, such as IV fluids and exchange transfusions, etc., are provided according to standards that ensure patient safety.
 - Continual medical and other professional education are part of the centre's long-term programme
 - Staff/patient ratio is defined arbitrarily and approximately as one doctor per 100 patients and one nurse per 50 patients.
 - In a multiorgan condition such as thalassaemia, assessment by various specialists is necessary, but decisions should be joint and tailored to individual patient needs in an integrated care setting [28,29].
- (6) Quality improvement
 - Suggestions for quality improvement are the responsibility of medical staff, nursing staff, and the administration.
 - Decisions should be based on information and performance data collected through monitoring and implementing policies [29].
 - Quality improvement is a systematic approach to changes aiming to upgrade services and correct any deficiencies in the service's governance, structure, and functions. Quality improvement aims to better the patient experience and outcomes by changing provider behaviour.
 - How change is introduced and implemented is a matter of concern and may require expert advice.
 - External influences, such as governmental policies or interests, budgetary support, and professional requirements, are considerations, and advocacy is a responsibility of all the team.
 - Setting goals, monitoring progress, and choosing the tools to bring about change. These could be skills development, computerisation, and updating guidelines, etc.
 - The patient's voice must be involved in all stages of quality improvement. Patients/families can also effectively monitor the effects and benefits of change since they experience the whole "patient pathway".
 - Studying other centres' experiences in change-making and understanding whether such changes have been successful elsewhere is necessary.
- (7) Information management
 - Patient records (paper or electronic) are kept with due consideration to confidentiality, security, and accuracy of data.

- The retention time of records in a haemoglobinopathy setting is lifelong, since the current clinical condition may be influenced by past events and disease control (such as iron levels).
- Standard diagnosis codes are kept (e.g., ICD10).
- E-health systems are assessed and tested for quality and patient safety before implementation.
- There is clear identification of those authorised to enter data and access patient records.
- Protection against loss, unauthorised access, or its use is ensured.
- Policies and procedures concerning record keeping are clearly directed to all the staff, through documents and training.
- The patient should be clearly identified on each record, with at least two identifiers.

4. Discussion

The principles described can be regarded as issued for consideration in an accreditation process such as that described by the International Society for Quality in Healthcare (ISQua) [<http://isqua.org> (accessed on 22 December 2022)]. Our survey found such an accreditation in only 2/20 centres located in lower-middle-income countries. The reasons are manifold and include poor and interrupted financial resources and political instability, with frequent changes in authorities and decision-makers at the ministerial level. Such instability affects continued political interest and prioritisation of haemoglobin disorders, even in situations where they are prevalent and constitute a visible public health problem. This applies also to any quality improvement effort in the experience of TIF in such countries, the majority of which are in the LIMC category. Progress and problem-solving are slow and often interrupted [20,30], yet the quality of care is intimately related to outcomes in these lifelong conditions [31,32]. It is noted that the “hub and spoke model” requires both organisation and dedicated physicians. As such, it should be politically recognised as an essential support system for rare conditions with complex pathologies and provided with a financed infrastructure. It is, in fact, the model suggested by the European Reference Network system that has resulted in the creation of the EuroBloodNet and other networks in support of rare disease patients.

It has long been recognised that the needs of patients, both clinical and social, with chronic disorders such as these cannot be met by periodic visits to acute care facilities [31]. Multimorbidity develops over time and requires an integrated care model to efficiently and effectively produce the desired outcomes for patients. In fact, the technical efficiency of thalassaemia centres has rarely been studied [33]. By setting standards in this TIF model for reference treatment centres, the possibility of assessment and quality improvement to meet the standards becomes easier. In suggesting these standards, we have not included patient outcomes at this stage. An experienced centre should have evidence of good patient survival and meet criteria such as the percentage of patients with a ferritin level <1000 µg/L, a percentage of patients keeping cardiac and hepatic MRI T2 heart T2* below a certain level, or DAA availability for hepatitis C treatment and others. It is considered that at this point in time these outcomes are not clearly defined, and we could not make recommendations in the text. TIF has considered such standards in its “Global Review of Services” published online on its website. Further research is needed to confirm such clinical outcomes as standards for healthcare services, including further discussion among experts.

One aspect not discussed in this study is whether participation in screening and counselling as part of prevention should be a criterion for centre expertise. In most countries, prevention policies and activities are taken over by the central government at ministry level as national programs, even though the centres may play an active role, especially in family and carrier counselling. However, as this service is variable, we did not include it as criterion.

From these thoughts, the concept of accreditation becomes a central consideration. It has been adopted by general hospitals even in low-income countries [34]. Accreditation

of highly specialised centres as separate entities from the public hospital is a challenge, often complicated because many hospitals hosting such centres are without accreditation. In addition, the unique needs of specialised centres must be recognised by administration and health authorities/policymakers.

Setting standards for haemoglobinopathy centres, as described above, has allowed the TIF advisory group to develop a checklist for the assessment of centres (see annex in Appendix A). This list has been piloted in two centres, one located in a high-income country and the other in low-middle-income country. The basis of an accreditation programme for haemoglobinopathy centres from this pilot study has been developed.

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Appendix A

ANNEX: Elements of Assessment (each of these are given graded points according to availability and practice).

1. Description of Centre: Name and detailed address.
2. Governance: Administrative authority (e.g., government, university etc), scientific advisory committee, and financial sustainability.
3. Staffing: Staff names, ages, qualifications, and experience in haemoglobinopathies; administrative director, clinical director, and organisational chart of key personnel with qualifications and specialties (including medical specialists offering multidisciplinary support, nurses and social support). Staff/patient ratios.
4. Patients: Total number, numbers by diagnosis, age distribution. The existence of a patient registry (whether paper-based, electronic, local or part of a regional or national registry, legal/ethical regulations kept in data sharing, data protection (e.g., patient consent, data transferred using encryption, transferred only to centres which also comply with security standards).
5. Health system: Universal coverage, voluntary blood donation.
6. Infrastructure: Building/spaces/functional areas according to patient needs facilitating patient journey, patient registration, transfusion rooms according to patient age groups, playroom for children, recreation room for adults, resuscitation room and equipment, treatment room, storage facilities, doctors' consultation rooms, and nursing station.
7. Patient services: (a) Working hours of the centre with the aim to maximise patient benefit. (b) Patient information: Full explanation given to patients concerning their medical condition; dietary advice; a research project in which patient data are used; concerning volunteering for clinical trials, including risks and benefits; and informed written consent for involvement in any treatment or research. Patient involvement is necessary in advisory committees, clinical decision-making that concerns them, encouraged in self-management. (c) Patient wellbeing: Availability and psychological care impacts on adherence to long-term treatment and, thus, survival. Beneficial approaches as identified in the literature include group sessions, family therapy, and patient camps. To be beneficial for the patients, expert psychological support has to be tailored to children's needs, adolescents, and adults, as a service offered with multifaceted care. Dental care, nutritional status, and neurological sensory assessment are not neglected.
8. Centre's involvement in teaching and research.

9. Clinical care: (a) Evidence-based guidelines: The centre operates based on evidence-based guidelines, which means that international levels of care are adopted. (b) Basic equipment availability: Refrigerator for blood storage, filtration, infusion pumps, stadiometers, growth charts, electronic communication, transcranial Doppler, ECG, etc. (c) Blood bank providing uninterrupted supply of blood: This is evaluated by interruptions and/or delays in providing blood transfusions, allowing Hb levels to fall. (d) Investigation facility: Availability of sophisticated examinations for diagnosis and monitoring patient progress: Including phenotypic and molecular diagnosis of Hb disorders, MRI, MRI-T2*, Ferriscan, DEXA, Abdominal U/S. All monitoring is according to international guidelines (TIF) in terms of timing. (e) Multidisciplinary team: Specialised care, including at least cardiological, endocrinological, hepatological, gynaecological, and psychological specialists, within reach in the same hospital. Communication between specialists and clinic doctors with regular discussions of findings and common/agreed treatment options. (f) Blood transfusion: Extended antigen typing is important before the first transfusion in order to assist future detection of antibodies. ABO, Rh(D)-compatible blood is offered following careful crossmatch, matching for C, E, and Kell (strongly recommended). Collaboration of blood banks is essential. Leuko-depleted blood. Record of reactions and annual transfusion requirements. For TDT patients pretransfusion Hb 9–10.5 g/dL, with Hb 11–12 g/dL for patients with heart complications. (g) Iron chelation: Availability of all three iron-chelating agents along with peripherals (infusion pumps). Tailoring according to each patient's needs is practiced by experienced physicians. Effectiveness and possible side effects are monitored as described in the latest international or national guidelines.

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