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Recognizing Specialized Reference Centres for Haemoglobin Disorders and Promoting their Role in Developing Networks

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ABSTRACT

Haemoglobin disorders are genetic conditions which require complex and multidisciplinary services, challenging healthcare services in many countries. The objective is to provide optimum care to all patients, equally, wherever they may live in the world. The need for specialized centres was recognized early in haemogobinopathy management, as dedicated clinical services can help to reduce morbidity and prolong survival. Reference treatment centres follow guidelines and apply standards with evidence of good outcomes, including measures such as survival, morbidity and quality of life. Recognition is verified by inspection and data collection and is made official by accreditation which is acceptable by the administrative authorities. The Thalassaemia International Federation (TIF), as part of its mission to promote, in as many countries as possible quality care, has initiated a program to recognize collaborating centres and promote specialization, but also support to peripheral centres which may not have the experience or the means to serve patients with the same standards. This report describes principles and means with which these goals are promoted. At the time of writing 9 centres in 4 countries (in South Asia, Middle East and Europe), have volunteered and have been visited by teams of reviewers. Of these 7 have been recognized as TIF collaborating centres. These centres altogether serve 5750 patients with all haemoglobinopathies (65% with thalassaemia and 35% with sickle cell syndromes). Two more centres are currently under review.

Introduction

THE NEED FOR SPECIALISED REFERENCE CENTRES

Haemoglobin disorders are genetic conditions which are considered major public health issues in many countries, especially in low- and middle-income counties (LMICs) where prevalence is high[1]. Mutations in the globin gene result in abnormal globin chain synthesis causing the thalassaemias or abnormal structure which may result in serious conditions such as sickle cell disease. Clinical consequences include anaemia due to ineffective erythropoiesis and haemolysis[2] or polymerization of deoxygenated hemoglobin S and causing vaso-occlusion[3]. In both conditions multi-organ damage is the eventual consequence, requiring complex and multidisciplinary services. They are classified as benign haematology disorders as they are not cancerous, however they can be lethal early in life if not well treated from the earliest stages of life and require multi-faceted and quality services for best results.

Current data demonstrate that 7% of the global population carries a pathological Hb gene and more than 500,000 affected children are born annually[4] with varying degrees of anaemia and clinical severity. Alpha (α) and beta (β) thalassaemia, sickle cell disease, and other rare inherited anaemias, represent chronic conditions with challenging and difficult management requirements that demand a central policy both to provide comprehensive approach to management but also the choice of prevention as well as adequate budgetary support for services including, social and economic support to families.

The Thalassaemia International Federation (TIF) was founded with a vision and a mission which centres around the patients' welfare and the provision of optimum care to all patients, equally, wherever they may live. This remains TIF's patient centred focus today. The quality of care is central to achieving desired patient outcomes, including reduced morbidity and complications, good quality of life and long survival[5,6]. It is in this context that the Board of Directors has given a directive since 2017, for an initiative, whose aim is the recognition of a network of accredited collaborating centres which can provide clinical services to patients according to quality standards which can result in the best patient outcomes. This is a major undertaking requiring much thought and preparation. However, the benefits, based on evidence from internationally accepted standards, are reflected in improved patient outcomes. The objectives of the initiative:

1. To encourage quality in the service to patients and the development and proliferation of centres of expertise
2. To encourage networking between centres which fulfil standards of good clinical practice and support peripheral centres which may serve fewer patients or have limited services and expertise at their disposal. This means that patients residing far from centres able to provide optimal monitoring and care have the same chance of benefitting from expert care through sharing elements of care not available to all. By facilitating all patients' access to expert management, the aim is to contribute to the reduction of inequalities in the care that patients receive.
3. To use the collaborating centres to contribute to TIF's educational programmes, including clinical research. This includes providing educational and training outlets for the centre's staff as well as the staff of secondary/ peripheral centres. Providing the opportunity for continuing medical education.
4. To encourage centres in their capacity to advocate for policy development by government agencies in support of patients' unmet needs.
5. Provide authoritative scientific opinions and advice on key topics in clinical management including accurate diagnostic techniques, blood safety, correct iron monitoring, treatment of iron overload and dealing with complications through a multidisciplinary approach in order to achieve continuous improvement within

the healthcare delivery system for haemoglobinopathies worldwide.

6. Provide a mechanism for internal and external peer evaluation towards excellence of care and ensure each centre's accountability for the service they provide to patients
7. Improve patient safety in all activities and initiatives.
8. Provide networking opportunities through technology with other regional and international treating centres and benefit from tele-consultation and telemedicine in general, to enable stakeholders to promote quality services.
9. Enhance community confidence in thalassaemia care in all affected countries

This need for specialized centres was recognized early in haemogobinopathy management, as dedicated clinical services can help to reduce morbidity and prolonged survival[7,8].

The need to ensure expertise in dealing with complex or rare diseases and conditions was also recognized by the European Commission which encouraged member states to develop centres of expertise[9] and to have them linked in networks for improved sharing of best practices[10]. Recognition of the value of specialized centres has proliferated to developing countries[11]

WHAT IS QUALITY CARE

Even though health care professionals and services in general are motivated to achieve the highest outcomes in the care of patients, such services are not always supported to provide optimum care, which is patient centred, safe and results in the desired outcomes[12]. This is particularly so where chronic and rare diseases are concerned. Chronic diseases are a significant burden on health services and usually require long term, complex and multidisciplinary care models.

Health care quality is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes. Quality of long-term care is the degree to which services contribute to maximizing well-being and quality of life and increase the likelihood of personal and health outcomes that are consistent with the individual preferences, human rights and dignity of both care users and their caregivers[13]. In 1999, the Institute of Medicine (IOM) released six domains to measure and describe quality of care in health[14, 15].

Table 1. Based on IOM, quality in health care should be:

1	Safe	Avoiding injuries to patients from care that is intended to help them
2.	Effective	Avoiding overuse and misuse of care.
3.	Patient-Centered	Providing care that is unique to patients' needs
4.	Timely	Reducing waiting times and harmful delays for patients and providers.
5.	Efficient	Avoiding waste of equipment, supplies, ideas and energy
6.	Equitable	Providing care that does not vary across intrinsic personal characteristics

In practice the processes towards achieving these aims are:

- Identifying treatment centres that actually follow guidelines and apply standards with evidence of good, including measures such as survival, morbidity and quality of life. Recognition is verified by inspection and data collection and is made official by accreditation which is acceptable by the administrative authorities.
- Within the health system to officially recognize the communication and support given to the staff and patients of peripheral or smaller centres.

Accreditation

Accreditation provides public recognition that a service provider meets standards of quality set forth by an accrediting agency. Organizations seek accreditation for different reasons but most do so in an effort to win customer satisfaction and professional reputation.

The International Society of Quality in Health Care (ISQua) (18) defines accreditation as:

"…self-assessment and external peer review process used by health care organizations to accurately assess their level of performance in relation to established standards and to implement ways to continuously improve the health care system. Quality standards and the external peer review process are directed by nationally recognized autonomous, independent accrediting agencies with a commitment to improve the quality of health care for the public".

Methodology

TIF is not an official accrediting agency. However, TIF's vision is to promote, in as many countries as possible, the hub and spoke model so that patients can benefit from specialised tests (such as MRI), which may not be available in their periphery, and benefit from expert opinion. For such a system to be effective, it should be created under the approval and administrative support of health authorities, who must regulate the relationship between the supporting centre and the 'secondary' centres (which may be large hospitals with only few thalassaemia patients). Communication means, such as sharing medical information (electronic or otherwise) and patient travel may need to be supported.

As currently practiced, TIF recognizes centres which meet standards as expressed in international guidelines, as being collaborating centres in TIF's policies which aim to improve patient care. This is facilitated by collaboration with local experts and organisations while official recognition from the countries health authorities is also sought. Apart from supporting peripheral centers, at this stage the main focus is the promotion of collaborating centers as education and training centers, and the promotion of technology sharing.

All patients should ideally be supported by a universal health coverage system. At the same time specialized centers require a financial investment and support but by offering expertise and specialised tests and reducing morbidity they are a more economic model in the long term.

The standards required for TIF recognition are included in assessment tools or questionnaires, which are attached in annexes I, II and III. These questionnaires were constructed based on the EUCERD standards[8,9].

A TIF Collaborating Reference Centre for Haemoglobinopathies is expected to comply with the following standards:

- Appropriate governance, adequate workforce with training and expertise in case management and sustainability. Any previous recognized accreditations (such as ISO, JCI) are an added value
- Has appropriate capacity to diagnose, follow-up and manage patients, with evidence of good outcomes, based on TIF International Guidelines for the Management of Transfusion-Dependent Thalassaemia and other similar standards. Outcomes are assessed by measures such as age distribution of the patient population, complication rates, mortality rates and health related quality of life
- Has sufficient capacity to acquire experience and provide expert advice and to implement outcome measures and quality control
- Demonstrates a multi-disciplinary approach to clinical management, including psychosocial support
- Has high level of expertise and experience documented through staff experience, publications, grants or honorary positions, teaching and training activities
- Demonstrates active contribution to research

- Is involved in epidemiological surveillance, and maintains registries and good medical records
- Maintains close links and collaboration with other expert centres at the national and international levels and a capacity to network
- Holds close links and collaboration with patients' associations where they exist.

At the same time the physical design and the spaces of the day care center are considered; doctors offices, nurses stations, day care, inpatient wards, patients' facilities (children, adolescents and adults) and rooms for guests are examples of a dedicated center's facilities. Patient reported outcomes and assessment tools are important considerations in the final assessment.

In case the performance of the center does not fully meet expectations, the certifying body will make recommendations for improvement and will re-assess performance after two years.

Some health facilities have already an accreditation certificate e.g. JCI but this should not prevent further certification by TIF of the special services diseases specific i.e. addressing haemoglobin disorders in particular.

Recognition of collaborating centres for haemoglobin disorders, comes through a process of accreditation. This implies that a service centre has been recognized as meeting established standards of quality and safety through both self-assessment and external peer assessment. Meeting such standards is an important driver for safety and quality improvement and is not just a snapshot of current services but also an ongoing process of quality improvement. Standards of care are based on evidence based best practices, laid down in guidelines and are usually disease specific, even though some common principles are also considered.

The following steps for assessment are followed in the TIF accreditation process:

- Treatment centers are invited to apply to become collaborating centers and are short listed for a programmed visit
- Pre-visit self-assessment questionnaire is offered to candidate centers. This is then examined by a team of experts and those assessed to be eligible are candidates for a visit which is then planned
- A small team of experts, usually 2 from the TIF group of medical advisors, themselves experienced clinicians in recognized centers of expertise, is chosen for the onsite visit. They may also be accompanied by an expert patient.
- The visit is programmed and usually lasts 2 working days
- The questionnaires in annex I-III are used as guidelines. Questionnaire I is the pre-visit self-assessment tool while QII is guide for team not to miss any important information during the visit. The third questionnaire is directed to patients who are treated in the candidate centre and aims to mine patient feedback on the services offered.
- The patient journey in the center is followed, from registration to triage, to transfusion where indicated, waiting areas and relaxation facilities; the quality of treatment areas and any safety concerns noted (patient identification, hygiene, resuscitation facilities etc). Barriers to access, including language and cultural issues are investigated.
- Governance, sustainability, mission and official support are noted
- Staff adequacy in numbers and education are listed. Low staff turnover is appreciated to ensure experience and specialization. It is expected to see educational programs and tools in place for continuous development of competencies of the more junior in experience staff.
- Patient numbers and staff/patient ratio is also considered.
- Monitoring and management of complications through multidisciplinary involvement is imperative

- A written report from the visiting team is provided to the TIF Board of directors with final recommendations from the visiting experts
- For the successful centres a certificate is issued which lasts for 2 years and can then be renewed. A plan of common activities is then planned between TIF and the collaborating centre
- For centres which do not fulfill the criteria, there follows a discussion on all the aspects for improvement detected and optimising measures are discussed both with the staff and the governing authority as appropriate.

Additional issues in favour of the services offered include working hours that consider patient involvement in education and employment; whether the centre is networking with other centres; electronic records are also an added value; universal health coverage with no or minimal out of pocket expenses, is an advantage as is the consideration of social concerns.

Results

In a pilot project initiated in 2017-18, 2 centers were visited. Since then the first center has provided training for staff from another country and has also since been reinstated. To date 9 centres in 4 countries (in South Asia, Middle East and Europe), have volunteered and have been visited by teams of reviewers. Of these 7 have been recognized as TIF collaborating centres. These centres altogether serve 5750 patients with all haemoglobinopathies (65% with thalassaemia and 35% with sickle cell syndromes).

Discussion

Whether the principles discussed are utilized in the services for haemoglobinopathy care, it has not been widely investigated, since most published reports are from academic centers and do not often describe the wider picture to reflect the quality of services which serve the majority.

Quality in Healthcare in a complex multi-organ condition like thalassaemia, is achieved through the use of standards, protocols, guidelines and other management tools[16]. A set of standards comprises a list of standardized requirements in terms of quality-assuring infrastructure and processes that a healthcare organization has to fulfil. Measures such as age distribution of the patient population, morbidity and mortality data and health related quality of life can be used to describe outcomes and reflect the quality of services.

Clinical management of these conditions is marked by inequalities in the quality of patient care across the world, resulting in poor outcomes for the majority of patients. To address these inequalities, it requires often community and professional intervention. The policy of creating centres of expertise and providing means of communication and support with secondary centres is an effective means of meeting this goal. This means that routine blood transfusions and medications can be provided peripherally while the patients are able to visit the reference centre which would hold the overall responsibility of care, at intervals as dictated by their condition for detailed assessment and management decisions. This hub and spoke model has been put into practice in the EU through the ERNs (European Rare Disease Networks) in the last few years; these are 'virtual networks connecting healthcare providers across Europe to tackle rare, low-prevalence, and complex diseases[17].

The centres recognised so far are not meant to define the 'best' centres in a country, but only those which currently are collaborating in joint projects with TIF, having voluntarily applied to be assessed and to partake in commonly agreed projects. Nevertheless, they are examples of centres which can be considered as care models by others within a country and abroad. It is hoped that local or national governments, under whose jurisdiction these centres come, will recognize and appreciate that their services and standards have been recognized by international experts. Other centres in the country should also enquire into the standards of care that were evaluated in

these centres and adopt such standards in their own services. In this way there will be a proliferation of good practices and more patients overall will benefit.

In this description we have not discussed each clinical criterion and standards in detail. The basis of all criteria is patient welfare and good clinical outcomes. The rights of patients and patient-centered care, are at the core of all efforts towards quality improvement of clinical services. Few healthcare systems monitor and set standards for chronic disease management. So, centers of expertise are not often officially recognized. Shared care is a culture that has not been widely applied. Auditing performance and peer reviews are ultimately the only means to establish effective quality, patient centered care with continuous improvement of care delivery and patient experience.

The TIF's vision of organizing and implementing a quality program in healthcare centers treating patients with Thalassaemia and other haemoglobinopathies, is a challenge which requires the support of the federated associations members of TIF in each country, as well as the healthcare professionals involved. It is of paramount importance that appropriate standards, protocols and guidelines are adhered to in order to secure comprehensive care with the highest possible level of quality. In addition, new approaches to treatment including curative treatments, are already available in some high income countries. The technological infrastructure to practically apply these innovative approaches means that centers with the capacity to offer high standards of care is a necessary step in all countries. With no centers of appropriate expertise in all countries, inequities will always be a shadow over patient care.

Patient satisfaction is an important part of the TIF assessment's process and so patient reports on their experiences in the center is of vital importance. The patient's journey at each visit, the visiting hours and their possible interference with education and employment must be considered. Patient centered care demands consideration of these life activities of patients who are obliged to visit the center as often as every 2 weeks. In addition, the increasing experience of population and cultural diversity through population migration is making new demands and is increasing the need for 'cultural competence'[19].

The level of support from the healthcare system of the country is a vital component affecting the quality of services. At the level service delivery recognition by the competent authorities of reference centres with practical financial and administrative support. At the level of patient care, issues such as universal health coverage and minimal out of pocket expenses for such life-long conditions along with psychosocial support are imperative considerations for best outcomes. Policy makers must, with these considerations in mind, be alerted by both the medical and patient communities to recognize the need for centers of expertise leading in the field of quality care.

References:

1. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Organ. 2001;79(8):704-12.

2. Sanchez-Villalobos M, Blanquer M, Moraleda JM, Salido EJ and Perez-Oliva AB (2022) New Insights Into Pathophysiology of b-Thalassemia. Front. Med. 9:880752. doi: 10.3389/fmed.2022.880752

3. Sundd P, Gladwin MT, Novelli EM. Pathophysiology of Sickle Cell Disease. Annu Rev Pathol. 2019 Jan 24;14:263-292. doi: 10.1146/annurev-pathmechdis-012418-012838.

4. Piel FB. The Present and Future Global Burden of the Inherited Disorders of Hemoglobin. Hematol Oncol Clin North Am. 2016 Apr;30(2):327-41. doi: 10.1016/j.hoc.2015.11.004.

5. Forni GL, Gianesin B, Musallam KM, Longo F, Rosso R, Lisi R, Gamberini MR, Pinto VM, Graziadei G, Vitucci A, Bonetti F, Musto P, Piga A, Cappellini MD, Borgna-Pignatti C; Webthal® project. Overall and complication-free survival in a large cohort of patients with β-thalassemia major followed over 50 years. Am J Hematol. 2023 Mar;98(3):381-387. doi: 10.1002/ajh.26798.

6. Delicou S, Manganas K, Diamantidis MD, Venou TM, Delaporta P, Pantelidou D, Spachiou E, Tsagia S, Pappi V, Petropoulou F, Kapsali E, Evliati L, Papaioannou K, Katsatou M, Klironomos E, Vasiliadi A, Gkoutzouvelidis A, Giasari P, Zisis C, Lafiatis I, Goula A, Xydaki A, Papadopoulou D, Chatzoulis C, Lafioniatis S, Vini D, Serpanou A, Kalkana C, Kyriakaki S, Drandaki M, Kouraklis A, Kattamis A, Vlachaki E. Comparative analysis of mortality patterns and treatment strategies in thalassaemia and sickle cell disease patients: A 12-year study. Br J Haematol. 2025 May;206(5):1466-1478. doi: 10.1111/bjh.20043

7. Forni GL, Puntoni M, Boeri E, Terenzani L, Balocco M. The influence of treatment in specialized centers on survival of patients with thalassemia major. Am J Hematol. 2009 May;84(5):317-8. doi: 10.1002/aj h.2 1398.

8. Angastiniotis, M.; Eleftheriou, A.; Naveed, M.; Assaf, A.A.; Polynikis, A.; Soteriades, E.S.; Farmakis, D. TIF Standards for Haemoglobinopathy Reference Centres. Thalass. Rep. 2023, 13, 10-20. https://doi.org/10.3390/thalassrep13010002

9. EUCERD Recommendations on quality criteria for Centres of Expertise for Rare Diseases (24 October 2012): http://www.euserd.eu/upload/file/EUCERDRecommendationCE.PDF

10. EURORDIS Position paper – European Reference Networks for Rare Diseases (May 2012): http://www.eurordis.org/[ublications/european-reference-networks-rare-diseases

11. Khurana R, Kanvinde P, Ganatra P, Bodhanwala M, Aggarwal B, Mudaliar S. Impact of Dedicated Thalassemia Day Care Services: Pediatric Hematologist's Perspective. Indian J Hematol Blood Transfus. 2025 Jan;41(1):102-106. doi: 10.1007/s12288-024-01817-8.

12. Wagner EH, Bennett SM, Austin BT, Greene SM, Schaefer JK, Vonkorff M. Finding common ground: patient-centeredness and evidence-based chronic illness care. J Altern Complement Med. 2005; 11 Suppl 1:S7-15. doi: 10.1089/acm.2005.11.s-7.

13. Promoting quality management in long-term care: principles, key components and directions for policy action. Copenhagen: WHO Regional Office for Europe; 2024. Licence: CC BY-NC-SA 3.0 IGO. Document: WHO/EURO:2024-10957-50729-76831, https://iris.who.int/bitstream/handle/10665/379697/WHO-EURO-2024-10957-50729-76831-eng.pdf?sequence=1

14. Institute of Medicine (US). Committee on quality of health care in America. Crossing the quality chasm: a new health system for the 21st Century. Washington, D.C: National Academies Press; 2001.

15. Ku, G. M. V., van de Put, W., Katsuva, D., Ahmed, M. A. A., Rosenberg, M., & Meessen, B. (2024). Quality of care for chronic conditions: identifying specificities of quality aims based on scoping review and Delphi survey. Global Health Action, 17(1). https://doi.org/10.1080/16549716.2024.2381878

16. Musallam KM, Cappellini MD, Porter JB, Farmakis D, Eleftheriou A, Angastiniotis M, Taher AT. TIF

Guidelines for the Management of Transfusion-Dependent β-Thalassemia. Hemasphere. 2025 Mar 5;9(3):e70095. doi: 10.1002/hem3.70095.

17. https://health.ec.europa.eu/rare-diseases-and-european-reference-networks_en

18. Guidelines and Principles for the Development of Health and Social Care Standards 4th Edition Version 1.2, September 2015. https://isqua.org/media/attachments/2018/03/20/guidelines_and_principles_for_the_development_of_health_and_social_care_standards__4th_edition_v1.2.pdf

19. Saha S, Beach MC, Cooper LA. Patient centeredness, cultural competence and healthcare quality. J Natl Med Assoc. 2008 Nov;100(11):1275-85. doi: 10.1016/s0027-9684(15)31505-4.

