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Review Article

Genetic Counselling in Haemoglobinopathies: another Duty for Nurses and Midwives?

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Abstract

Haemoglobin disorders are caused by mutations which affect the quantity or the functionality of the haemoglobin molecule. The main clinical syndromes that result from such mutations are sickle cell disease (SCD) and beta thalassaemia (both transfusion dependent and non- transfusion dependent). It is estimated that 5-7% of the global population are carriers of such genes and 3560000 new affected births being added annually (all syndromes). These figures are indicative of a considerable burden on health services especially in low resource countries where they are most prevalent. Population management and screening policies are for this reason adopted by many countries. Screening programmes to identify carriers who are usually asymptomatic. Genetic counselling follows the identification of carriers, especially carrier couples at-risk for having affected offsspring. Qualified genetic counsellors are scarce and so doctors, midwives and nurses are called upon to take on this responsibility. Without training, are these clinicians aware of the complexities and possible pitfalls of counselling ? Is knowing the clinical aspects of management and outcomes enough to answer any question that a couple may have concerning impact of a potential diagnosis, outcomes of current therapies and possible future developments which may modify outcomes? With these facts in mind the Thalassaemia International Federation proposes that a course to train healthcare providers including nurses to train in all the aspects of effective counselling.

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Introduction

Haemoglobin disorders are a group of hereditary anaemias, caused by mutations which affect the quantity or the functionality of the haemoglobin molecule. These are mutations on the genes that regulate the protein part of the molecule, mainly the α- and the β-globin genes [1]. The main clinical syndromes that result from such mutations are sickle cell disease (SCD) and beta thalassaemia. The latter are divided into transfusion dependent thalassaemia (TDT) and non-transfusion dependent (NTDT) which include beta thalassaemia intermedia, HbH disease (alpha thalassaemia) and HbE/ beta thalassaemia. These categories reflect the spectrum of severity of these syndromes and due to this spectrum, both clinical management and family planning decisions are affected. They are all characterised by varying degrees of anaemia, ineffective erythropoiesis and iron overload. These effects are more pronounced in β-thalassaemia [2]. In the case of sickle cell disease apart from anaemia, the sickling of red cells under conditions of reduced oxygenation causes vaso-occlusive episodes resulting in tissue anoxia and organ damage [3].

The more severe TDT requires daily medications, regular blood transfusions and lifelong monitoring for new organ complications and multidisciplinary interventions. In the 'milder' conditions there is initially either no need for treatment or reduced management requirements; over time however, even in these mild syndromes, complications will arise so that only childhood seems to be trouble -free. The quality of monitoring and management ultimately determines the survival and quality of life. TDT is lethal from infancy if not treated early with blood transfusion; it also results in premature death at any age including poor quality of life if treatment is not according to evidence-based guidelines [4,5].

Survival, along with good clinical practices, also depends on genomic factors. The issue of genotype/phenotype and clinical severity is a sensitive one in counselling since final decisions on choices (marriage, family planning) can be influenced by both the counsellor's and the couple's understanding of what is acceptably 'mild' or unacceptable. The fact that mild initially may progress to serious co-morbidities in later life must be explained to prospective partners or parents.

Premarital couples would wish to understand the clinical outcomes and how these are influenced by standard treatment modalities and whether prognosis will change in the near future with the introduction of new therapies. All these are factors which can influence future parents in their choices and so the counsellor must be prepared to answer questions. The perceived effects on well-being and social integration, affecting the patient and the family environment are also factors which influence decisions so a psychosocial sensitivity by the counsellor is factor in quality of counselling [6,7]. These all require in-depth knowledge of these disorders and a high level of counsellor education.

In addition, consideration of the cultural, religious and legal background of the community and especially the individuals being counselled is important since these considerations influence their

understanding of what is being said as well as their final decisions. The cultural diversity is due to the wide geographical distribution of haemoglobin disorders; these may be common in some indigenous populations, while rare in other societies but increasing due migrations [8].

It is estimated that 5-7% of the global population carry a gene affecting the production or quality of the haemoglobin molecule. About 56000 new affected births with beta thalassaemia are expected annually with living patients which should exceed 1 million if alpha thalassaemia is added [9]. Sickle cell syndromes are even more prevalent, since there are about 300 000 annual affected births globally, most of them in sub-Saharan Africa [10]. These numbers are indications of significant burden, social as well as health-wise, to many healthcare systems across the world. Policies for disease awareness and management are for this reason adopted by many countries [11,12].

Policies have been developed over many years and the components or strategies, include the following [12]:

- A national policy on prevention which indicates national approval, control and support
- A public awareness programme, sensitising the people on an issue that may affect their reproductive life and explaining the need for timely screening
- A screening programme to identify carriers who are usually asymptomatic
- Genetic counselling services, provided usually by doctors, occasionally by nurses and rarely by qualified genetic counsellors
- Prenatal diagnosis as a choice for at risk couples
- Preimplantation genetic testing as an alternative choice
- New emerging technologies, such as non-invasive prenatal diagnosis

Genetic counselling for haemoglobin disorders

Definition and Purpose

Counselling means to educate, inform and support individuals or couples in making informed choices. Choices available for couples at risk [12]:

Risk identified Choices

Before marriage or pregnancy

1. To avoid marrying another carrier
2. To separate from a relationship that puts their future children at risk
3. To marry their chosen partner despite knowing the risk

After marriage or cohabitation

1. To proceed with a pregnancy accepting the risk of an affected child
2. To avoid having biological children (includes choosing adoption or donor gametes)
3. To accept going though prenatal diagnosis, choosing to either accept an affected child or to terminate the pregnancy
4. To use pre-implantation genetic diagnosis as an alternative to prenatal diagnosis and so avoid termination of pregnancy

When already pregnant

1. Choose to go through prenatal diagnosis (if in early pregnancy)
2. Accept any outcome with no further action
3. Terminate the current pregnancy with no further action

Information/education that the counsellor is expected to provide, depending on the background of the individual or couple, or the questions that may be asked by these individuals (language and terminology may vary according to the couple's education), are expected to be of several categories:

Background information introducing haemoglobinopathies or the particular syndrome that affects them:

- What is haemoglobin, why is it important to the human organism and what are consequences of reduced or altered function of the molecule. What are haemoglobin disorders?
- The recognised pathogenic variants on the globin genes and their significance in genotype/ phenotype relations. The counselees may have with them laboratory results which they hope will be explained. Knowledge of the screening algorithms, and the laboratory tests performed. These include the haematology results, but the molecular tests may be more challenging to explain.
- An explanation on what being a carrier (heterozygote) means to the individual's health and future prognosis. This is particularly relevant to sickle cell carriers since extreme environmental factors (cold, altitude, anoxia) and exercise may have an effect on their health.
- Information on inheritance pattern and implications to family members. Family considerations are central to genetic counselling; prompt consideration of cascade screening (genetic screening of relatives who may also be carriers) may support individuals in their decisions.

Clinical aspects of Hb disorders. Basic discussion should include

- Description of the clinical consequences of the condition affecting the counselee. This includes the treatments available (how is thalassaemia or SCD treated? What are the treatment options and what is available? Is it curable? Are there prospects of new treatments?). What is the prognosis of no treatment, affordable treatment and optimal comprehensive care. A further discussion on the impact of the condition within a social and legal context is also essential for individuals to make fully informed decisions.
- There is a spectrum of severity: can the counsellor know wherether severity can be predicted in a given family in terms of mild conditions needing little or no treatment, versus disease that requires daily and lifelong interventions? The issue of genotype/phenotype and clinical severity is a sensitive one in counselling since final decisions on choices (marriage, family planning) can be influenced by both the counsellor's and the couple's understanding of what is acceptably 'mild' or extremely severe. The fact that mild initially may progress to serious co-morbidities in later life must also be explained to prospective partners or parents.

Modes of inheritance

Estimation of genetic risk for parents and family members is a basic function of counselling. This requires drawing a family tree. It may also call for investigations on other family members. The common form of inheritance of β-thalassaemia and sickle cell disease is the recessive mode.

The basic modes of inheritance must be explained. It should be remembered that there are concerns which need further explanation, such as the effects of double heterozygosity and the interaction of genes. Rare cases of dominant beta thalassaemia may occur (so a counsellor must be well aware of the unusual). Also, Alpha (α-) globin chains are produced by four genes; one or more of those can be changed or missing altogether so if a child inherits only one functional α-globin gene and three are missing then clinically significant HbH disease is the diagnosis; if all four genes are missing then Hydrops Fetalis, (also known as Hb Bart's syndrome or as α-thalassaemia major) which causes a severe anaemia that affects the foetus.

Ethical, Cultural, and Communication Considerations

1. Communication skills: these include active listening, unconditional positive regard privacy, patience, empathy, non directiveness and trust building.

2. Ethical principles must be pointed out and elaborated: Confidentiality, the non-directive approach leading to informed choice. The psychosocial and family factors that can influence choices must be understood by the counsellor. The autonomy of the couple must be respected and their suggestion that the counsellor should decide must be avoided [13].

3. Cultural considerations: being sensitive to the religious and culture influences that may affect a couple's choice. This requires knowledge of various cultures but also the ability to explore the couple's beliefs. Avoiding being critical of prejudices [14].

4. Language can be a major consideration since messages may not be clearly understood by either side. A translator may be needed but must not be a relative. Further aids such as visual and digital tools may enhance communication.

5. Repetition of the session may be necessary since the first announcement of genetic risk may be emotionally tense making complicated concepts difficult to engulf at the first consultation. Adequate post-counselling engagement through written information (letter, leaflets, links to validated websites) can help individuals process complex information.

6. Information on risks to family members are part of the genetic counselling process. Individuals and couples may be offered information that can help their relatives and are encouraged to communicate openly with family members. It is known this communication may be impacted by cultural and societal pressures and the clinician needs to be considerate of this dimension.

7. Consanguinity- advantages and disadvantages must be discussed if a couple is related. Autosomal recessive diseases are more frequent in the offspring of these couples. How closely related they are will determine the proportion of genes shared between them. So, a careful drawing of a family tree will help in estimating the share of genes and the likelihood of a homozygote birth [15].

8. Where premarital testing is offered, an at-risk couple may consider separation. In some societies they are in fact urged to separate and are issued incompatibility certificates if both are carriers. Nevertheless, even in these situations it is for the couple to decide whether to proceed with marriage, free of any influences [16].

9. Prenatal diagnosis – methods, risks and complications must be discussed so that the couple may choose to accept the test with full knowledge of benefits versus risks. If the fetus is found to be affected the choice facing the parents will lead to the question of possible termination of pregnancy. This is a painful decision for any couple in any culture but in some cultures, it meets with legal as well as religious obstacles. Counsellors have to be supportive of any decision the couple takes, ensuring informed choice [17,18]

10. Pre-implantation genetic diagnosis – risks, costs religious acceptance to be discussed [19]. One sensitive issue to be discussed with parents who already have an affected child is the choice of an embryo for implantation which is not only disease free but also can be an HLA compatible donor for its affected sibling [20].

11. Where α-thalassaemia is concerned, there two main issues must be considered:

a. The question of whether prevention of HbH disease, which in many populations is compatible with long survival without treatment is in fact necessary; the more severe forms of course the choice of prevention is clearer.

b. Intra-uterine treatment of hydrops can be offered explaining the postnatal dependence on blood transfusion [21].

Discussion and Recommendations

Who provides counselling: Counselling is for all the reasons described above, a complex and private service. It should be offered by the professional who understands the condition, its natural history, treatment and complications, as well as the mode of inheritance. Ideally this is a service that should be offered by trained and qualified counsellors [22,23].

On a global such qualified and registered counsellors are rare in clinical services. In 2023, it was estimated there were 10,250 genetic counsellors globally, practicing in over 45 countries [24]. Most of them are practicing in the western world where haemoglobin disorders are relatively rare conditions. Where these disorders are prevalent in the indigenous population, such specialised counsellors are indeed hard to find. In practice, counselling for these conditions, to serve patients and families as well as carriers for family planning, is carried out either by the haematologist, the obstetrician, the paediatrician, nurses or laboratory staff.

The counsellor nurse is usually one that has specialised and has worked for some time in haemoglobinopathy clinics. Often, she replaces the doctor who has limited time for the necessarily long counselling sessions. In addition, many individuals or couples leave the consultation with the doctor feeling uncertain since the language used was too 'technical' or 'scientific' and the nurse is approached to elucidate. The role of nurses in counselling is not new [25,26] and as a consequence the training of nurses in genetics and especially in the developing field of genomics, has become a significant issue [27,28].

Since counselling is offered by various healthcare specialties, patient, parents or at -risk couples education and counselling requires familiarity with all issues described above [29]. These include understanding of the social, legal, religious and moral issues that arise in counselling, with cultural sensitivity alongside a deep understanding of the science and testing modalities. Can a clinician or a nurse without guidance, promote informed choices and adaptation to the complex lifelong experiences that the condition entails.

The Thalassaemia International Federation TIF, has experienced many instances of poor communication. The impact of counselling, depends on several factors, including how the audience will interpret the information provided. This can be influenced by education and culture, trust in the informant, but also by emotional factors. For example, choices such as choosing a partner may be particularly difficult in societies where arranged marriages and consanguinity are customary. A relationship of trust has to be cultivated. This can be achieved if the counsellor indicates that he/she is interested in matters beyond purely medical and that social and other factors can be discussed and brought into the open free of judgement. Understanding issues such as anxiety, guilt, blame, fear; which influence the couple's or individual's coping ability, including the ability to understand risk can be detrimental in engaging in a productive and supportive conversation.

Few of these factors are taught to the physician or other health provider, with the exception of the medical geneticist or the qualified genetic counsellor. This is a major concern especially the commonality of haemoglobin disorders is realised and is increasing through migration and population growth.

With these facts in mind TIF proposes that a course to train healthcare providers, particularly nurses and midwives in all the aspects of effective counselling. Nurses and midwives as previously stated are best chosen from the ranks of specialised haemoglobinopathy nurses, since experience of the disease and its medical and social consequences is vital. However, such training for the whole field of genomics as well as counselling is essential for all nurses and midwives. The art of active listening, and empathy cannot easily be taught but these are essentials for successful and effective counselling.

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