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# Genetic counseling for individuals with hemoglobin disorders and for their relatives: a systematic literature review

ACONSELHAMENTO GENÉTICO PARA INDIVÍDUOS COM ALTERAÇÕES DAS HEMOGLOBINAS E SEUS FAMILIARES: REVISÃO SISTEMÁTICA DE LITERATURA

ASESORAMIENTO GENÉTICO PARA INDIVIDUOS CON ALTERACIONES DE LAS HEMOGLOBINAS Y SUS FAMILIARES: REVISIÓN SISTEMÁTICA DE LITERATURA

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## ABSTRACT

**Objective:** To identify genetic counseling programs that do not encourage therapeutic abortion for individuals with hemoglobin disorders and/or for their relatives.

**Method:** Systematic literature review of articles published from 2001 to 2012 that are located in the PubMed, LILACS, SciELO and SCOPUS databases using keywords in Portuguese, English and Spanish and that met the inclusion and exclusion criteria described on a standardized form. **Results:** A total of 409 articles were located, but only eight (1.9%) were selected for analysis. **Conclusion:** Although seldom mentioned in the literature, educational/preventive programs targeting hemoglobinopathies are feasible and allow the affected individuals to acquire knowledge on the consequences of this condition and their odds of transmitting it.

## DESCRIPTORS

Genetic counseling  
Hemoglobinopathies  
Disease prevention  
Health education  
Review

## RESUMO

**Objetivo:** Identificar programas de aconselhamento genético sem incentivo ao aborto terapêutico para indivíduos com alterações das hemoglobinas e/ou seus familiares. **Método:** Revisão sistemática de literatura realizada nas bases de dados PubMed, LILACS, SciELO e SCOPUS por artigos publicados de 2001 a 2012, utilizando descritores em português, inglês e espanhol, de acordo com formulários padronizados contendo critérios de inclusão e exclusão. **Resultados:** Dos 409 estudos encontrados somente oito (1,9%) foram selecionados. **Conclusão:** Os programas de educação/prevenção para hemoglobinopatias, embora raramente encontrados na literatura, são possíveis e permitem que indivíduos adquiram conhecimento sobre as consequências de seu distúrbio e a probabilidade de transmiti-lo.

## DESCRIPTORES

Aconselhamento genético  
Hemoglobinopatias  
Prevenção de doenças  
Educação em saúde  
Revisão

## RESUMEN

**Objetivo:** Identificar programas de asesoramiento genético sin incentivo al aborto terapéutico para individuos con alteraciones de las hemoglobinas y/o sus familiares.

**Método:** Revisión sistemática de literatura realizada en las bases de datos PubMed, LILACS, SciELO y SCOPUS por artículos publicados de 2001 a 2012, utilizando descriptores en portugués, inglés y español, según formularios estandarizados que abarcaban criterios de inclusión y exclusión. **Resultados:** De los 409 estudios encontrados solo ocho (1,9%) fueron seleccionados. **Conclusión:** Los programas de educación/prevenção para hemoglobinopatías, aunque rara vez encontrados en la literatura, son posibles y permiten que los individuos adquieran conocimiento acerca de las consecuencias de su disturbio y la probabilidad de transmitirlo.

## DESCRIPTORES

Asesoramiento genético  
Hemoglobinopatías  
Prevención de enfermedades  
Educación en salud  
Revisión

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## INTRODUCTION

Hemoglobinopathy is a group of disorders caused by substitutions, insertions or deletions in the coding regions of the  $\alpha$  and/or  $\beta$  globin chain genes<sup>(1)</sup>. The clinical manifestations of these disorders exhibit quite a broad scope and are characterized by striking differences in severity<sup>(2)</sup>. Episodes of pain are the most recurrent among such manifestations and might result in stress, anxiety, depression, frequent hospital admissions and suffering for both patients and their relatives. The most severe cases are associated with productivity loss and socioeconomic, emotional and psychological problems<sup>(3-4)</sup>.

Approximately 7% of the world population currently exhibits symptoms of hemoglobinopathies<sup>(5)</sup>. It is estimated that 4% of the Brazilian population is heterozygous for sickle cell anemia (sickle cell trait) and that 25,000 to 50,000 individuals exhibit some type of hemoglobinopathy<sup>(6)</sup>. This high prevalence of hemoglobinopathies emphasizes the need for educational preventive actions by means of community-based programs for early diagnosis, information, education and communication<sup>(7)</sup>.

Genetic counseling is a process of communication regarding human problems related to the occurrence or risk of recurrence of genetic disorders within families<sup>(8)</sup>. This process is used by counselors to help patients and families interpret the results of tests; to provide information on heredity, prevention, resources, diagnosis and follow up; and to promote informed decision-making and adaptation to the conditions of risk<sup>(9)</sup>.

Genetic counseling plays a crucial role in the promotion of public health and human rights<sup>(10)</sup>. In the countries in which abortion is allowed in cases of fetal abnormalities, to preserve the mother's health or for socioeconomic reasons<sup>(11)</sup>, genetic counseling might encourage the termination of high-risk pregnancies as an approach to reduce the incidence of hemoglobinopathy<sup>(12)</sup>. In Brazil, where therapeutic abortion is prohibited, genetic counseling appears to seldom be provided to families with hemoglobinopathies and is mostly performed in the neonatal period for the purpose of diagnosis and family planning or at blood donation centers<sup>(13)</sup>.

In the current genomic era, however, genetic counseling, including its broad scope of genetic information but without encouraging therapeutic abortion, plays a crucial role in primary care, as it allows for counselors and their patients to engage in the search for preventive measures<sup>(14)</sup>. Thus, the aim of the present study was to identify genetic counseling programs that do not encourage therapeutic abortion for individuals with hemoglobinopathies and for their relatives by means of a systematic literature review.

## METHOD

A systematic literature review was performed of scientific articles published from 2001 to 2012 located in the PubMed, LILACS, SciELO and SCOPUS databases to answer the following question: are individuals with hemoglobinopathies and/or their relatives provided genetic counseling without encouraging therapeutic abortion following clinical and laboratory-based diagnosis? Several keywords were tested in the attempt to answer this question, and the best combination was *sickle cell anemia*, *thalassemia*, and *genetic counseling* (*anemia falciforme*, *talassemia* and *aconselhamento genético* in Portuguese and *anemia de células falciformes*, *talassemia* and *asesoramiento genético* in Spanish), as located at the Virtual Health Library using the controlled vocabulary thesaurus DeCS (Descritores em Ciências da Saúde/Health Science Keywords) and PubMed using MeSH (*Medical Subject Headings*) (MeSH). Except for PubMed, which allows combining several keywords in searches, the terms were combined in pairs in the remainder of the databases to ensure that all of the relevant articles would be included for analysis.

The articles found were subjected to relevance tests using standardized forms composed of inclusion and exclusion criteria (Chart 1). The abstracts of the articles were analyzed first by means of relevance test I, and the articles considered to be potentially relevant for the present systematic review were subjected to relevance test II, which targeted the full text of the articles.

Articles published in English, Portuguese or Spanish from 2001 to 2012 that describe genetic counseling for individuals with sickle cell anemia or thalassemia or for individuals heterozygous for those conditions were selected for analysis. A manual search was performed based on the references cited in the selected articles to include relevant articles that could have been missed.

The articles were independently assessed by two examiners. Any instances of disagreement as to the inclusion or exclusion of studies were resolved by consensus.

**Chart 1** – Form for relevance tests I and II

FORM FOR RELEVANCE TEST I		
Inclusion criteria	Yes	No
1. Does the article address genetic counseling for individuals with hemoglobinopathy or for individuals heterozygous for this condition?		
2. Does the study mention any type of orientation, information or educational actions for individuals with hemoglobinopathy or for individuals heterozygous for this condition?		
3. Genetic counseling was not performed in the study, but the individuals with hemoglobinopathy or individuals heterozygous for this condition were referred for specialized services.		
Exclusion criteria	Yes	No
1. Is the article an editorial, letter, review or comment?		
2. Did genetic counseling encourage abortion?		
Reason for inclusion or exclusion:		

Continued...

FORM FOR RELEVANCE TEST II		
Inclusion criteria	Yes	No
1. Were sickle cell anemia and thalassemia included among the investigated hemoglobinopathies?		
2. Were the individuals with hemoglobinopathy or individuals heterozygous for this condition given genetic counseling?		
3. Were the individuals with hemoglobinopathy or individuals heterozygous for this condition referred to genetic counseling services?		
Exclusion criteria	Yes	No
1. Did genetic counseling encourage abortion?		
2. Was genetic counseling used for the general population?		
3. Did the study only address the relevance of genetic counseling?		
4. Are the data reported in the article insufficient for analysis?		
Reason for inclusion or exclusion:		

## RESULTS

Based on the search criteria and keywords used, 409 articles were located in the investigated databases. Following the application of relevance test I, 345 articles were excluded according to the established inclusion and exclusion criteria, and 64 articles were considered as potentially relevant for the aims of the present review. The full text of those 64 articles was read and subjected to relevance test II, which resulted in the exclusion of another 56 articles. As a result, only eight articles were included for systematic analyses (Figure 1).

**Chart 2** – Studies on genetic counseling for hemoglobinopathies published from 2001 to 2012 that were selected for the present systematic literature review

Author (publication year)	Study location	Period of data collection	Study population	Participants (no.)
Memish (2011) <sup>(15)</sup>	Saudi Arabia	2004–2009	Couples at risk for hemoglobinopathies	8,925 couples
Kladny et al. (2011) <sup>(16)</sup>	United States	2003–2009	Families of individuals heterozygous for hemoglobinopathies	300 families
Souza et al. (2010) <sup>(17)</sup>	Brazil	2001–2005	Families of newborn infants with hemoglobinopathies	29 families
Farra et al. (2008) <sup>(18)</sup>	Lebanon	2005–2007	Mothers of children with thalassemia	97
Tazari et al. (2007) <sup>(19)</sup>	Gaza Strip	2003–2005	Couples at risk for thalassemia	19
Diniz and Guedes (2005) <sup>(20)</sup>	Brazil	2001	Blood donors heterozygous for sickle cell anemia	100 <sup>a</sup>
Karetti et al. (2004) <sup>(21)</sup>	London	1998	Individuals with $\beta$ -thalassemia (trait or case)	28
Viana-Baracioli et al. (2001) <sup>(22)</sup>	Brazil	12 months <sup>b</sup>	Pregnant women with abnormal hemoglobin	68

a. Number estimated based on data provided by the author – 10 sessions with approximately 10 participants each.

b. Authors did not indicate the year in which the study was conducted.

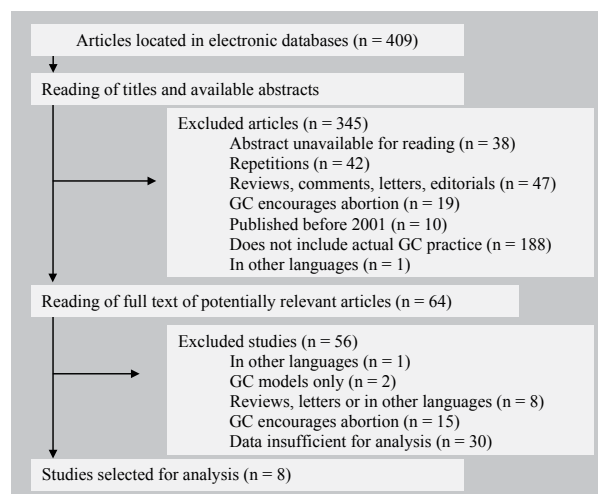
**Chart 3** – Aims and strategies of the authors relative to the provision of genetic counseling for hemoglobinopathies in studies published from 2001 to 2012 and selected for the present systematic literature review

Author (publication year)	Aim	Strategy	Main approach
Memish and Saeedi (2011) <sup>(15)</sup>	To estimate the impact of hemoglobinopathies and to assess the frequency of detection and prevention of at-risk couples	Diagnosis and genetic counseling	Explanation of test results and of the risks of the union of at-risk couples
Kladny et al. (2011) <sup>(16)</sup>	To investigate the impact of genetic counseling on families of heterozygous individuals	Pre-counseling (letters), diagnosis and genetic counseling (sessions with counselor)	Explanation of test results, basic concepts of genetics and heredity and relevance of diagnosis
Souza et al. (2010) <sup>(17)</sup>	To assess the effectiveness of neonatal screening programs	Diagnosis and genetic counseling for families	Explanation of test results

Continued...

The characteristics of the included articles are summarized in Chart 2. Although the studies included different populations, most authors, who were from several different countries, agreed that genetic counseling including information/education ought to be provided to individuals with hemoglobinopathy and to their relatives as well as to individuals liable to transmit altered genes to their offspring.

Although the authors of the included studies employed various genetic counseling strategies, the purpose of the counseling was similar: to prevent the occurrence of hemoglobinopathies and to promote awareness of this subject (Chart 3).



**Figure 1** – Process of inclusion and exclusion of articles in the present systematic review (GC: genetic counseling)

Author (publication year)	Aim	Strategy	Main approach
Farra et al. (2008) <sup>(18)</sup>	To assess the acceptance of preimplantation genetic diagnosis	Diagnosis and genetic counseling for families	Basic concepts of genetics and the explanation of risks and complications of preimplantation diagnosis
Tazari et al. (2007) <sup>(19)</sup>	To assess mandatory performance of pre-nuptial testing	Diagnosis and genetic counseling	Explanation of test results, heredity, couple compatibility
Diniz and Guedes (2005) <sup>(20)</sup>	To demonstrate the relevance of genetic counseling at blood banks	Diagnosis, pre-counseling (letters) and genetic counseling	Information on sickle cell trait when individuals donate blood or seek reproductive care
Karetti et al. (2004) <sup>(21)</sup>	To assess the efficacy of genetic counseling	Genetic counseling	Basic concepts of genetics and heredity and relevance of diagnosis
Viana-Baracioli et al. (2001) <sup>(22)</sup>	To prevent the occurrence of hemoglobinopathies through the study of patients' families	Dissemination in the media; diagnosis and genetic counseling for patients and families	Explanation of test results and relevance of diagnosis

## DISCUSSION

The results of the present review show that several scientific articles published from 2001 to 2012 correlated genetic counseling and hemoglobin disorders; however, only eight (1.9%) referred to genetic counseling that does not encourage abortion. The reason for that small number of articles might be that genetic monitoring of individuals with hemoglobinopathies began only very recently. This fact also accounts for the decision of a large proportion of authors to address several other aspects of genetic counseling, such as its relevance, the need to establish specific programs for this purpose and the successful models that should be reproduced, but without actually providing genetic counseling. In addition, the aim of genetic counseling in many countries is to reduce the incidence of hemoglobinopathy through therapeutic abortion.

Currently, non-directive genetic counseling is better accepted, as it takes the psychological and social issues of the individuals into consideration. Presently, psychosocial genetic counseling is not only based on the future reproductive decisions of an individual but also on a concern for the education, culture, personality and values of patients and their relatives to help all of them adjust to the risk of occurrence/recurrence of disease<sup>(23)</sup>. In addition, within the context of that model, counselors attempt to help patients choose the best possible option based on their personal perspective while avoiding steering them into any particular direction<sup>(24)</sup>.

Overall, although the studies included in the present review had quite different designs and methods, all of them emphasized the relevance of providing genetic counseling to patients with hemoglobinopathy and to their relatives. The authors emphasized that preventive programs using information-, education- and communication-based methods are feasible and allow for individuals to acquire knowledge of the consequences of hemoglobinopathies, the odds of transmitting them and the available options for family planning.

Thus, the key elements for the prevention of hemoglobinopathies are information, laboratory diagnosis and genet-

ic counseling. In addition, genetic counseling should not be coercive but should enable the affected couples to make an informed decision and ensure their reproductive freedom<sup>(25)</sup>.

The efficacy of the educational process might be centered on the identification of individuals with hemoglobinopathy through neonatal screening<sup>(26)</sup> or any other diagnostic resource<sup>(27)</sup> followed by the provision of information, which provides countless benefits to families, such as the possibility of future reproductive choices, awareness of the relevance of the status of individuals with this disease and the advancement of genetic knowledge. Most parents of children with sickle cell anemia who were provided genetic counseling increased and maintained their knowledge about the disease, particularly when counseling was performed by specialized services<sup>(26)</sup>.

Several proposals were observed in the present review, such as the selection of unaffected embryos for later implantation<sup>(18)</sup>, which is advocated as an option for the Palestinian community as a result of its high prevalence of  $\beta$ -thalassemia and religious restrictions. At-risk couples from that same area are also suggested not to conceive children<sup>(19)</sup>.

It is worth noting that the investigators who conducted the three Brazilian studies included in the present review<sup>(17,20,22)</sup> chose screening and genetic counseling services. This observation demonstrates that the educational process is an essential tool for the prevention of genetic diseases in Brazil, where abortion is prohibited.

Due to the high prevalence of hemoglobinopathies in Brazil and the need to provide genetic counseling, Ruling no. 1,391<sup>(28)</sup> from 2005 established the promotion of access to information and genetic counseling for families and individuals with sickle cell disease or traits within the framework of the Unified Health System (*Sistema Único de Saúde* - SUS). This type of encouragement policy might serve as a model of prevention for other countries in which therapeutic abortion is prohibited, as it is in Brazil.

Several actions aimed at controlling hemoglobinopathies might be incorporated into the public primary care setting. Among such actions, the following stand out: pop-



ulation and family screening, multidisciplinary and multi-professional follow up and access to services specialized in genetic counseling<sup>(10,12-13,29)</sup>.

Although training and additional resources are needed, genetic counseling should be implemented in the public healthcare system as a program to ensure access to healthcare for individuals with hemoglobin disorders. The benefits are considerable, as genetic counseling decreases the morbidity and mortality and reduces the financial costs associated with this condition, improves the quality of life of patients, prevents complications and sequelae and helps all of the affected individuals to make informed decisions about their reproductive future.

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## CONCLUSION

The present systematic review showed that few individuals who are homozygous or heterozygous for hemoglobinopathies from several countries have been provided genetic counseling to date, although the implementation of preventive actions has paramount importance. Thus, these findings establish the need to implement a larger number of genetic counseling programs that do not encourage therapeutic abortion in an attempt to demonstrate that this type of intervention might help individuals affected by or homozygous for hemoglobinopathies to better understand aspects that are crucial for disease management and for family planning.

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