DOI: 10.32385/rpmgf.v39i1.13435

National newborn screening for sickle cell disease and communication of carrier status

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ABSTRACT

Portugal recently implemented a pilot project to screen for Sickle Cell Disease during national newborn screening. This project started in Lisbon and Tagus Valley region, where there is a higher frequency of African descendants. With the expansion of this screening to the rest of the country, a question arises: how to deal with cases of Sickle Cell Trait?

Keywords: Sickle cell disease; Sickle cell trait; Carrier state; Neonatal screening; Communication.

Sickle cell disease (SCD) is a severe non-malignant disorder inherited in an autosomal-recessive manner.[1-2] SCD is most prevalent in malaria-endemic areas such as Sub-Saharan Africa, the Middle East, and India. SCD is a major cause of childhood morbidity and mortality in these areas.[1-3] Though, timely access to penicillin antibiotic therapy and pneumococcal vaccination significantly reduce the number of lifelong vaso-occlusive events.[4-7] This therapeutic benefit supports the implementation of newborn screening (NBS) for SCD in Western European countries.[1-2,4] In the 90s, Portugal tried to implement a screening program for SCD, carrying out a pilot study centred on a maternity hospital in Lisbon.[2,5] The low number of identified carriers at the time and the lack of identification of any patient affected with SCD hindered the expansion of screening to the rest of the country.[5] However, there has been a change of outlook in recent years in Portugal and the rest of Europe.[2] Cases of children with SCD and carriers are increasingly common all over the European continent due to increased migration for economic reasons from areas with a higher frequency of SCD.[2,4]

In Western European countries, NBS for SCD is either universal (UK, Spain) or restricted to regions with a high population of immigrant minorities (France, Belgium).[1-4] Error-prone selective screenings have the disadvantage of needing to discriminate the ethnicity of the parents and the possibility of missing affected children because of incorrect selection.[2,4] In addition, although parents provide consent for screening, no protocol exists for parents who refuse to participate.[2-3] Besides, any positive result obtained is confirmed by a second-tier test, and the screening is only considered positive if both results agree.[1-2,8] Note that all results obtained in the context of NBS do not correspond to confirmed diagnoses, so special care is needed when communicating these to family members or the medical team.[2,8]

Historically, sickle cell trait (SCT) is considered a benign condition.[3,6,8-9] Although people with SCT are considered asymptomatic (having often mild anaemia or haematuria), more recent studies indicated that people with SCT may have a two-fold higher risk for chronic kidney disease, as well as a moderately elevated risk for thromboembolic events (similar to that

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described for factor V Leiden or the G20210A variant of prothrombin gene). These studies have also identified a higher risk for rare clinical outcomes such as exertion-related injury, splenic infarction, or renal medullary carcinoma.[2-3,6,8-9] So much so that these potential complications have forced American adolescents and young adults to clarify their carrier status before participating in high-competition sports or endorsing military service.[3,9] Elsewhere, the identification of carriers allows to carry out family reproductive options.[2,4-5,10] This last point is controversial as no child should be screened for future family planning without their prior consent.[9-10] Furthermore, it is questioned whether the disclosure of this type of information compensates for the anxiety and mental health issues that some families feel after disclosing these results.[4,9-10] Another concern that should not be neglected is the burden of health services resul-ting from the identification of these carriers during screening. De Montalembert *et al.* calculated that for a birth rate from 0.6 to 3.6% of carrier babies in France, it is necessary to give about 4,000 to 5,000 couple consultations per year in a genetic counselling setting.[4]

Currently, there are no standardized methods for reporting positive SCT results to physicians or family members (primarily because NBS was not initially designed for reporting cases of carriers).[2-3,8] For example, in France, SCT results are communicated by letter three months after birth, with genetic counselling thereafter.[4] In the USA, the carrier status is communicated to primary care providers, who are responsible for reporting and advising families about it.[3,8-10] Canada chooses not to actively communicate the screening result unless parents expressly request it.[6] German Genetic Testing Act, on the other hand, vehemently prohibits the communication of carrier states to healthy minors, and only a clarification of what it means to be a carrier can reframe the importance of these findings.[1-2] Something similar is happening in Portugal, with the recent inclusion of the pilot study of SCD under the national NBS. According to Portuguese law (Lei nº 12/2005, January 26), there is no legal background that allows a healthy child's carrier status to be communicated to their parents or legal guardians. However, the same law states that health information is patients' property.[11] Previous reports have suggested that parents prefer to know their children's carrier status and that medical doctors feel obliged to report these results.[2,6]

Lastly, we should not disregard the cultural and religious beliefs of the communities to whom the carrier result is conveyed.[4] For example, in 2003 a royal mandate in Saudi Arabia required couples to be screened for SCD before marrying. Subsequent studies concluded that screening results did not significantly influence the couple's reproductive choices.[3] It is also known that the stigmatization of the disease is greater against women, as most African men believe that blood diseases are exclusively transmitted by women. The negative view of the carrier status can still force many couples to remain in the country to which they emigrated to receive what they consider to be the best possible care, breaking family ties with their communities of origin.[4]

In conclusion, NBS of SCD is highly recommended given its benefits in terms of reduced morbidity and mortality.[4] Unlike SCD, the rare complications associated with SCT do not meet the criteria required for inclusion as a medical condition in a NBS program. Nevertheless, the carrier status is reliably identified by the screening and can be considered a by-product of the NBS program (haemoglobin electrophoresis – a usual method used in the screening for SCD – can clearly distinguish a case of SCD from a carrier). The period immediately following NBS is ideal for primary care providers and clinical geneticists to educate affected families about potential health complications and reproductive considerations.[2]

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AUTHORS' CONTRIBUTIONS
Conceptualization, DFR; methodology, DFR; investigation, DFR; writing – original draft, DFR; writing – review and editing, LV e PL; visualization, DFR; supervision, LV e PL; project administration, DFR.

CONFLITO DE INTERESSES
Os autores declaram não possuir quaisquer conflitos de interesse.

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Recebido em 08-01-2022
Aceite para publicação em 08-06-2022

RESUMO

O RASTREIO NACIONAL NEONATAL DA DREPANOCITOSE E A COMUNICAÇÃO DO ESTADO DE PORTADOR
Portugal implementou recentemente um projeto para a inclusão da Drepanocitose nas patologias rastreadas no âmbito do Programa Nacional de Rastreio Neonatal. Numa fase inicial, este projeto limitou-se aos habitantes da região de Lisboa e Vale do Tejo, onde residem em maior número os indivíduos de ascendência africana em solo português. No entanto, considerando que este rastreio foi, entretanto, alargado ao restante território nacional, uma questão se levanta: como lidar com os resultados dos portadores de traço falciforme?

Palavras-chave: Drepanocitose; Heterozigoto HbS; Portador; Rastreio neonatal; Comunicação.