P-046 FACTORS ASSOCIATED WITH LEG ULCERS IN CAMEROonian SICKLE CELL DISEASE PATIENTS

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Purpose: Leg ulcers are the most common skin complication in sickle cell patients. Though it is associated with great morbidity and cost of care, research is rather sparse on this condition. Through this study, we wished to determine the factors associated with leg ulcers in sickle cell patients in two hospitals in Douala.

Materials and methods: This was a retrospective cross-sectional study carried out over a period of 05 years (January 01, 2015 to December 31, 2019). This study was carried out at two sites: the outpatient hematology department of the General Hospital Douala and Sickle cell care center at the LaQuintine hospital Douala. We included all sickle cell patients aged 10 years and above. We excluded patients with incomplete files. Data on sociodemographic characteristics and clinical and laboratory parameters were collected. Analysis was done using SPSS version 25.0 software. Qualitative variables were compared using Pearson’s chi-square test. Multivariate analysis was done using logistic regression to determine the factors associated with leg ulcers. Significance level was set at p <0.05.

Results: Out of 620 sickle cell patients, 41 (6.6%) had a leg ulcer. The median age of patients with a leg ulcer was 28 years (IQR 22-33). The male to female sex ratio was 1.15. Leg ulcers were traumatic in 70.7% of cases. The leg ulcer was unique in 65.85% (n=27) and located next to the malleolus in 26 (63.34%) of patients. Sociodemographic characteristics significantly associated with leg ulcers were the age groups 30-39 years [OR=9.3 (3.1-27.3), p <0.001], 20-29 years [6.3 (2.3-17.1), p <0.001] and a history of leg ulcer [2.7 (1.1-6.4), p=0.020]. For clinical characteristics, pulmonary hypertension [3.5 (1.7-6.7), p <0.001] and aseptic osteonecrosis of the femoral head [1.5 (0.01-22.5), p=0.020] were significantly associated with leg ulcers.

Conclusion: In the pathogenesis of leg ulcer, a triad of mechanical obstruction of the microcirculation, hemolytic-vascular dysfunc tion syndrome and venous incompetence has been incarcerated. In our study, one out of fifteen patients with sickle cell disease in Douala has a leg ulcer. Factors associated with leg ulcers were age between 20-39 years, pulmonary hypertension, aseptic osteonecrosis of the femoral head and history of leg ulcer. These factors are probably the result of chronic hyperhemolysis in our population.

The authors do not declare any conflict of interest

P-047 PROSPECTIVE IDENTIFICATION OF VARIABLES AS OUTCOMES FOR TREATMENT (PIVOT): A PHASE II CLINICAL TRIAL OF HYDROXYUREA FOR CHILDREN AND ADULTS WITH HBSC DISEASE

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Purpose: A substantial number of patients with sickle cell disease (SCD) have HbSC disease, especially those living in West Africa. HbSC may cause less early morbidity and mortality than sickle cell anemia (HbSS/S0), but individuals with HBSC disease suffer from the same complications and have reduced quality of life. Retrospective data suggest some benefits of hydroxyurea treatment for people living with HBSC disease, but rigorous prospective evidence is lacking. There are several subcategories of clinical outcomes, which we wish to determine the factors associated with leg ulcers in sickle cell patients. Through this study, we wished to determine the factors associated with leg ulcers in sickle cell patients in two hospitals in Douala.

Materials and methods: This was a retrospective cross-sectional study carried out over a period of 05 years (January 01, 2015 to December 31, 2019). This study was carried out at two sites: the outpatient hematology department of the General Hospital Douala and Sickle cell care center at the LaQuintine hospital Douala. We included all sickle cell patients aged 10 years and above. We excluded patients with incomplete files. Data on sociodemographic characteristics and clinical and laboratory parameters were collected. Analysis was done using SPSS version 25.0 software. Qualitative variables were compared using Pearson’s chi-square test. Multivariate analysis was done using logistic regression to determine the factors associated with leg ulcers. Significance level was set at p <0.05.

Results: Out of 620 sickle cell patients, 41 (6.6%) had a leg ulcer. The median age of patients with a leg ulcer was 28 years (IQR 22-33). The male to female sex ratio was 1.15. Leg ulcers were traumatic in 70.7% of cases. The leg ulcer was unique in 65.85% (n=27) and located next to the malleolus in 26 (63.34%) of patients. Sociodemographic characteristics significantly associated with leg ulcers were the age groups 30-39 years [OR=9.3 (3.1-27.3), p <0.001], 20-29 years [6.3 (2.3-17.1), p <0.001] and a history of leg ulcer [2.7 (1.1-6.4), p=0.020]. For clinical characteristics, pulmonary hypertension [3.5 (1.7-6.7), p <0.001] and aseptic osteonecrosis of the femoral head [1.5 (0.01-22.5), p=0.020] were significantly associated with leg ulcers.

Conclusion: In the pathogenesis of leg ulcer, a triad of mechanical obstruction of the microcirculation, hemolytic-vascular dysfunction syndrome and venous incompetence has been incarcerated. In our study, one out of fifteen patients with sickle cell disease in Douala has a leg ulcer. Factors associated with leg ulcers were age between 20-39 years, pulmonary hypertension, aseptic osteonecrosis of the femoral head and history of leg ulcer. These factors are probably the result of chronic hyperhemolysis in our population.

The authors do not declare any conflict of interest

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P-048 INFLUENCE OF SEVEN GENETIC POLYMORPHISMS ON THE RESPONSE TO SICKLE CELL DISEASE THERAPY WITH HYDROXYUREA

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Purpose: Sickle cell disease (SCD) is a serious public health problem worldwide. Currently, hydroxyurea (HU) is the most widely used drug in SCD as it promotes a reduction in severity of sickle cell events, improves
hematological parameters and increases the quality and expectancy of life. Despite the evident benefits of HU, there is significant inter-individual variability in pharmacological response and genetic factors seem to be associated. Therefore, this study evaluated the individual variability of pharmacological response to treatment with HU, analyzing pharmacogenetic markers and hematological parameters of patients with not treated SCD and after treatment.

Materials and methods: 185 patients with SCD treatment (n=93) and without treatment (n=92) with HU followed at Fundação Hemominas of MG, Brazil were evaluated. The mean levels of hemoglobin (Hb), hematocrit, reticulocytes, global leukometry and fetal hemoglobin (HbF) were assessed before and after treatment. Patients were genotyped by real-time PCR (qPCR) for the polymorphisms G>T (rs1799983) and T>C (rs2070744) on the endothelial nitric oxide synthase (eNOS) gene, C>T (rs17399586) of arginase type 1 (ARG1) gene, A>C (rs766432) and G>A (rs4671393) of the B-cell lymphoma/leukemia 11A (BCL11A) gene, G>A (rs9960464) of the Urea Transporter (UTA) gene and A>G (rs2182008) of the Fms-related tyrosine kinase 1 (FLT1). The Ethics Committee has approved this study.

Results: The average age of patients was 15.8±11.13 years, among which 54% were men. Genotypic and allele frequencies for polymorphisms in the gene of eNOS (rs1799983: G=0.76; T=0.26; rs2070744: T=0.65; C=0.35), ARG1 (C=0.36; T=0.14), BCL11A (rs4671393: G=0.76; A=0.24; rs766432: A=0.76; C=0.24), UTA (G=0.61; A=0.39), and FLT1 (rs2182008: G=0.92; A=0.08) were in Hardy-Weinberg equilibrium and were similar to those found in other populations. In the group of patients treated with HU, those with the GT genotype for the polymorphism in eNOS gene had higher baseline Hb values when compared to GG patients (p=0.033). When patients were grouped according to HU response profile in “responders” (HbF ≥ 20%) or “non-responders” (HbF < 20%), it was found that those with the AC and CC genotypes in the BCL11A and GA gene in the UTE gene responded more effectively to drug treatment than patients homozygous for the most frequent allele. No significant influences were found related to other polymorphisms or the response to HU after analyses by logistic regression.

Conclusion: This study is pioneer in describing the frequencies of 7 polymorphisms in 5 candidate genes in a population of individuals with SCD treated with HU in the state of MG. The findings suggest that patients with the GT genotype in the eNOS gene (rs1799983) have higher Hb values and that the polymorphisms in the BCL11A (rs766432) and UTE seem to affect the hematological response to HU. Support: FAPÉMIG (APQ-02608-14, PPSUS/PAQ-03560-13) and UFJE. The authors do not declare any conflict of interest

P-049 A ROADMAP FOR DELIVERING A GLOBALLY ACCESSIBLE GENE THERAPY

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Purpose: The convergence of innovative biotechnologies is propelling the field of gene therapy with consequential implications for treating and curing genetic and infectious diseases globally. Although dozens of gene therapies for a broad range of disease areas are expected to receive regulatory approval worldwide over the next decade, patients are unlikely to receive equitable access to these medical breakthroughs. In particular, the sophisticated infrastructure required to deliver gene therapies poses critical challenges for low and middle-income countries (LMICs) seeking to integrate gene therapies into resource-constrained health systems. Without critical foresight and targeted investments across LMICs, gene therapies will perpetuate global health inequity.

Materials and methods: Using gene therapies for sickle cell disease and human immunodeficiency virus (HIV) in sub-Saharan Africa as use cases, this project examined the necessary infrastructure required for effectively and sustainably delivering gene therapies in low-resource settings. Data was obtained through a series of interviews with expert stakeholders from sub-Saharan Africa, Europe, and the US. Interviewees represented multiple sectors including hospitals and community clinics, gene therapy companies, manufacturing, patient advocacy and community engagement, technical training, and global health priority setting. Interviews were supplemented with an extensive literature review.

Results: An analysis of stakeholder interviews revealed the need for core infrastructure across seven thematic areas: research; engagement and education; facilities and manufacturing; information systems, workforce, regulation; and finance. Although assessed individually, these domains are interdependent, highlighting the need to invest in and co-develop across all areas simultaneously and synergistically.

Conclusion: Building the requisite infrastructure for delivering gene therapies is a multi-decade endeavour. This long horizon should not discourage immediate action; rather, it should be acknowledged and appreciated as an opportunity for strategic preparation assuring future success. By establishing and maintaining infrastructure across several thematic areas, countries can accelerate the development and delivery of gene therapies. Throughout this process, key steps should be taken to improve outcomes:

- **Engage communities early and often:** The process of providing gene therapies must be patient-centred. Involving communities in the design and implementation process will lead to effective therapies that are acceptable and accessible.
- **Leverage existing infrastructure:** Maximizing the impact of limited resources and removing redundancies requires integrated services, multi-use facilities, and increased coordination.
- **Collaborate internationally:** While countries in SSA build research capacity, promote private sector innovation and commercialization, and update regulatory frameworks, international collaboration will facilitate the exchange of scientific equipment, knowledge and training, and policy.
- **Improve and adapt iteratively:** The success of gene therapy hinges on iterative cycles of feedback between research and clinical deployment. Infrastructure should support the ability of scientific and societal findings to inform healthcare practices and regulations.

While this study focuses on gene therapy delivery and its requisite infrastructure, considerations of health systems strengthening should remain at the forefront. The delivery of gene therapies should expand to align with health priorities set by countries (e.g., attention to non-communicable diseases). A narrow focus on gene therapies can create vertical systems of planning, management, and monitoring and evaluation that are not suited for other health areas and do not maximize the use of limited resources. The authors do not declare any conflict of interest

P-050 UNDERSTANDING BARRIERS TO AND ENABLERS IN EMPLOYMENT FOR PEOPLE WITH SICKLE CELL DISORDERS IN ENGLAND

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Purpose: This paper reports on empirical research which was conducted in England in 2018-2020 before the COVID-19 pandemic. It involved trying to understand barriers and enablers to employment for people who have sickle cell disorder (SCD).

Materials and methods: The project worked with people with SCD, and two of their voluntary organisations, the Sickle Cell Society and OSCAR Sandwell as partners. It used a method of ‘democratic co-production’ and people with SCD led two focus group discussions to formulate and critique questions to ask about work and to share their understandings of what barriers and enablers to employment had been in their experiences. Then forty-seven individual interviews were conducted with people with SCD incorporating feedback from those focus groups.

Results: We found that work was about more than just employment for people with SCD who had to engage in self-management of their conditions and were contributing a lot to their families and communities. There were considerable barriers to access employment and once in employment people could face various forms of discrimination. However, reasonable adjustments for people with SCD in the workplace were relatively simple and inexpensive to put into practice. While people with SCD have a right to accommodations in the workplace they did not often understand legislation or how that affected things like disclosure or their rights.

Conclusion: We development an employment policy guide to aid employers and employees in the workplace in England. Post-COVID-19 we have also thought about how to apply this to flexible work and working from home. The authors do not declare any conflict of interest