Revista de Ciencias Médicas de Pinar del Río

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

REVIEW ARTICLE

Maternal fetal complications of sickle cell anemia in pregnant women: literature review

Santiago Xavier Peñarreta-Quezada[1], Karla Magaly Sánchez-Sánchez[1], Paulette Baymar González-Rojas[1] , Marcela Estefania Chalacán-Castro[1]

[1]Universidad Autónoma Regional de los Andes, Ibarra. Ecuador.

Received: August 20, 2025
Accepted: August 21, 2025
Published: August 22, 2025

Citar como: Peñarreta-Quezada SX, Sánchez-Sánchez KM, González-Rojas PB, Chalacán-Castro ME. Complicaciones materno-fetales de la anemia de células falciformes en mujeres embarazadas: revisión bibliográfica. Rev Ciencias Médicas [Internet]. 2025 [citado: fecha de acceso]; 29(S1): e6862. Disponible en: http://revcmpinar.sld.cu/index.php/publicaciones/article/view/6862

ABSTRACT

Introduction: the drepanocitosis is in the entire world one of the illnesses monogenic hereditary more communes, it is a dysfunction genetic recessive autonomic that characterized by a punctual mutation of the hemoglobin.
Objective: to evaluate the maternal and fetal complications of sickle cell anemia in pregnant women.
Methods: it was carried out a bibliographical revision in the period of January from the 2024 to January of the 2025, articles of available complete text were included, of the last 5 years in English and Spanish language. You proceeded to the search of the different scientific articles in the databases Pubmed, Google Scholar, Web of Science (WoS), Scopus, Europe PMC and Scielo.
Development: among the complications of the illness, they highlight in the mother the sharp thoracic syndrome, the preeclampsia, the crises vasooclusivas and a high risk of mortality; while in the fetus the restriction of the intra-uterine growth, the prematuridad and the intra-uterine death prevail. The integral handling includes specialized prenatal controls, prevention of infections, appropriate suplementación and therapies like transfusions of red globules, it has demonstrated to reduce these risks.
Conclusion: the anemia of falciform cells during the pregnancy represents a significant clinical challenge, associating with a fetal maternal substantial increment of complications. Advance as the therapy génica they offer promising perspectives when approaching the genetic cause of the illness. The combination of rigorous medical pursuit, education for the health and therapeutic innovation constitutes the angular stone for the treatment of this hemoglobinopatía.

Keywords: Sickle Cell Anemia; Complications; Pregnancy; Fetal.

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

INTRODUCTION

Sickle cell anemia or drepanocytosis is one of the most common monogenic hereditary diseases worldwide. It is a multisystem disorder caused by a mutation in a single gene, characterized by the presence of abnormally damaged red blood cells by hemoglobin S, a variant of adult normal hemoglobin.[1,2]

Additionally, it is an autosomal recessive genetic disorder, characterized by a point mutation of the β-globin, due to substitution of glutamic acid by valine at the sixth position of the codon that generates the characteristic hemoglobin S molecule of the disease.[3] The predominant genotypes that give rise to sickle cell anemia include Hb SS, Hb SC, Hb Sβ+-thalassemia and Hb Sβ0-thalassemia. Other rare forms include hemoglobin SD and hemoglobin SE.[4]

The World Health Organization (WHO) considers drepanocytosis a public health concern, to the extent of proposing the goal of reducing it by 50 % by the year 2025, especially among women of reproductive age, considering a vulnerable group. Around 5 % of the world population and more than 7 % of pregnant women suffer from hemoglobinopathies such as sickle cell anemia.[5]

The disease is characterized by polymerization of HbS, vasocclusion, and chronic hemolytic anemia that precipitate a cascade of pathological events leading to a wide range of complications. These processes include endothelial vascular dysfunction, nitric oxide deficiency, oxidative stress, inflammation, hypercoagulability, and platelet activation. These pathophysiological processes generate ischemia in various tissues and organs, causing pain and organ failure. Chronic complications are divided into two main groups: those related to large-vessel vasculopathy (cerebrovascular disease, pulmonary hypertension, and retinopathy) and those caused by progressive ischemic organ damage (autosplenectomy, bone disease, hepatic damage, and renal failure).

Regarding pregnancy, it has been shown that this hemoglobinopathy is negatively associated with maternal health and prenatal outcomes. Maternal complications are maternal anemia, infection, vaso-occlusive crises, preeclampsia, preterm birth, and higher cesarean section risk. Fetal complications are intrauterine growth restriction, preterm birth, abnormal fetal heart rate, and intrauterine fetal death.[6]

The prevalence of sickle cell anemia in the Black population of Latin America varies; in Cuba it is 6,1 %, Brazil 6,2 %, Costa Rica 8,1 %, Honduras 10 %, Mexico 11,2 %, Colombia 11,9 %, and Panama 16 %. Within a country, ethnic differences exist, related to the origin of migrations, with groups from areas of high haplotype prevalence or, conversely, low prevalence, leading to differences in the prevalence of hemoglobin S by migration.[7]

In Ecuador, the prevalence of drepanocytic anemia estimated from 2000 to 2013 was about 1 in 12,400 patients who come to emergency care, whether new cases or multiple admissions.[8] All of the above led to the present review, whose objective was to evaluate maternal and fetal complications of sickle cell anemia in pregnant women.

METHODOLOGY

A literature review was conducted from January 2024 to January 2025, including full-text articles available, from the last five years in English and Spanish. The search of the various scientific articles was carried out in PubMed, Google Scholar, Web of Science (WoS), Scopus, Europe PMC and Scielo. The keywords and Boolean operators used in the search were: ("sickle cell anemia"

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

OR "sickle cell disease" OR "sickle cell disease anemia" OR "sickle cell disorder") AND ("prevalence" OR "prevalence rates" OR "mortality and morbidity" OR "mortality" OR "natality" OR "birth rates"). Inclusion and exclusion criteria were defined to establish a scope and select the most current articles with the highest level of scientific evidence possible. Full-text works were considered. The information collected was analyzed among the investigators, considering biases and the internal validity of each study.

DEVELOPMENT

The study of maternal-fetal complications of sickle cell anemia in pregnant women projects several findings that deserve consideration. This disease, underestimated, has a profound impact on maternal and fetal outcomes, revealing important complications that notably affect their health. The results suggest that the most significant maternal complication is acute chest syndrome, being an important factor influencing this disease, it is 14 times higher than in pregnant women without sickle cell anemia; retained placenta is 10.2 times higher, as well as urinary tract infection is 9,2 times higher.[9]

Other complications found are: maternal death 7,2 times higher, pregnancy-induced hypertension is 4,8 times higher, Eclampsia is 3,8 times higher, Cesarean section of the lower segment is 3,7 times higher, prematurity is 3,4 times higher, postpartum hemorrhage is 3,2 times higher, spontaneous abortions are 2,9 times higher, while the complications with lower risk of occurrence are preeclampsia.[10,11]

Regarding fetal outcomes, the most significant is intrauterine growth restriction affecting 7,3 times more than in gestants without this hemoglobinopathy, followed by intrauterine fetal death 5,4 times higher, perinatal mortality is 3,3 times higher than in offspring of women without the disease, fetal distress occurs 3,2 times more, neonatal deaths are 2,9 times higher, finally, the complications with lower risk of occurrence are low birth weight, and a five-minute Apgar score <7.[10,11]

Regarding maternal complications by trimester of pregnancy, it is known that there is a higher risk of acute vaso-occlusive crises during pregnancy with an accumulated incidence rate of 14,3 % by the end of the first trimester and increasing to 35,4 %. The accumulated incidence rates of acute coronary syndrome increase from 1,7 % by the end of the second trimester and at the beginning of the third trimester, increasing even more at the time of delivery to 4,2 %. The an accumulated incidence of sepsis in the first trimester is 0,5 % and rises by the end of the postpartum period to 3,4 %. While the accumulated incidence of venous thromboembolism increased from 0,3 % to the end of the second trimester and by the end of the postpartum period to 2,1 %.[11]

Furthermore, it is essential to consider that proper control of sickle cell anemia during pregnancy improves the health of the mother and fetus, reducing complications such as acute chest syndrome, retained placenta, urinary infections, and maternal death, intrauterine growth restriction, and intrauterine fetal death.[12]

Drepanocytosis results in deformed red blood cells, hemolysis, and obstruction of blood vessels, with progressive organ damage. Currently, gene therapy has been considered to treat this disease, with the aim of replacing adult hemoglobin with fetal hemoglobin, which offers greater protection against disease complications. Gene therapy is an emerging modality of medical treatment, defined as the use of one or more genes to treat, prevent, or cure diseases, by

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

inserting new copies of a defective or missing gene into the patient's cells, using viral vectors to transport the genetic material. This technique has shown utility in both hereditary genetic diseases and acquired disorders.[13]

However, despite promising prospects of gene therapy in the treatment of sickle cell anemia, important challenges persist, including genetic, investigative, and bioethical aspects. It is essential to address potential ethical dilemmas, such as discrimination based on genetic characteristics, accessibility to treatments, and equitable implementation of these therapies.[14] Gene therapy leads to a significant improvement in quality of life and reduces patient suffering; its ethical value and potential benefit are undeniable.[15]

According to the systematic analysis of the Global Burden of Disease Study, 3,2 million people live with sickle cell anemia, 43 million people have the drepanocytic trait (i.e., are carriers of the mutation), and 176,000 die each year from related complications. These patients incur very high health-care costs, more than a billion dollars per year just in the United States, and life expectancy has a median of 45 to 58 years, compared with the general life expectancy in the United States of 78,2 years. [16]

Pain is the most frequent symptom and the one that generates the most costs to the health system, due to visits to the Emergency Room and theHospitalizations. These pain attacks vary in duration and can manifest in different parts of the body, but are most common in the bones; the spine, the lower limbs in adults, and in the form of dactylitis in infants or newborns. Acute attacks can be triggered by stimuli such as cold air or water, low humidity, dehydration, stress, alcohol consumption, and menstruation in women, and can last for days or weeks. Chronic pain is silent and constant due to sensitization of the nervous system. During the non-attack period, the patient may have pallor, jaundice, splenomegaly, low weight, and decreased hemoglobin levels.[17]

The cosimpliThe most common complications associated with sickle cell anemia are avascular necrosis, commonly in the hip and femur, and an increased risk of infections by capsulated microorganisms such as Streptococcus pneumoniae and Haemophilus influenzae secondary to functional asplenia. Regarding pulmonary complications, 93,5 % of the patients included had abnormalities in chest imaging, and among the most common alterations was acute chest syndrome.[18]

In addition toBeing the most frequent clinical manifestation of sickle cell anemia, vaso-occlusive crises are the main cause of mortality and hospitalization in these patients and one of the most common predictors of death. Typically, acute pain caused by vaso-occlusive crises is located in the lumbar region or extremities, although it can also appear in the thorax, abdomen and even be migratory. This pain is classified as: acute or chronic, somatic or visceral, unilateral or bilateral, localized or diffuse and can vary from mild, moderate to severe.[19] Regarding the preoperative management of these patients, it has been recommended to perform surgical procedures only when patients have hemoglobin levels between 10 and 11 g/dL.[20]

One ofThe mainstay of treatment is red blood cell transfusions, so 90 % of adults with this condition will receive at least one transfusion in their lifetime. The usefulness of transfusion therapy is explained, in part, by its improved blood flow, decreasing the number of sickle cells, and its association with a decrease in endothelial injury and inflammatory damage.[21,22]

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

However, red blood cell transfusion carries risks of adverse events such as alloimmunization, hemolytic reactions, acute hyperhemolysis, and iron overload. Additionally, as with any blood product, there are risks of anaphylaxis, minor allergic reactions, and pulmonary complications such as transfusion-related acute lung injury (TRA-LI) or circulatory overload (TACO), as well as transfusion-associated sepsis.[23,24]

The kingssultaTwo of these analyses highlight the importance of a comprehensive approach to addressing maternal-fetal complications in pregnant women with sickle cell anemia. Appropriate management, such as regular and specialized prenatal care, vaccinations, necessary supplementation, proper nutritional habits, emotional support, and education, can significantly improve the health of both mother and baby, helping pregnant women with this hemoglobinopathy cope with their pregnancy.

CONCLUSIONS

Sickle cell anemia during pregnancy represents a significant clinical challenge, associated with a substantial increase in maternal-fetal complications. In the mother, acute chest syndrome, preeclampsia, vaso-occlusive crises, and an elevated risk of mortality predominate; while in the fetus, intrauterine growth restriction, prematurity, and intrauterine death are predominant. Integrated management includes specialized prenatal care, infection prophylaxis, appropriate supplementation, and therapies such as red blood cell transfusions, which have been shown to reduce these risks. Although advances such as gene therapy offer promising perspectives by addressing the genetic cause of the disease, the combination of rigorous medical follow-up, health education, and therapeutic innovation constitutes the cornerstone for the treatment of this hemoglobinopathy.

BIBLIOGRAPHIC REFERENCES

1. Hazin-Costa MF, da Silva Aráujo A, Guerra GL, da Matta MC, Torres LC, Souza AI. Chemokines in pregnant women with sickle cell disease. Cytokine. [Internet]. 2019 Jan [citado: 01/03/2024]; 113: 195–9. Disponible en: https://doi.org/10.1016/j.cyto.2018.07.002

2. Piel FB, Steinberg MH, Rees DC. Sickle Cell Disease. Longo DL, editor. New England Journal of Medicine [Internet]. 2017 Apr [citado: 01/03/2024]; 376(16): 1561–73. Disponible en: http://www.nejm.org/doi/10.1056/NEJMra1510865

3. Baralis Aragón P, Bonilla Álvarez G, Ye Ng LYM. Drepanocitosis en embarazo. Rev. Medica Sinergia. [Internet]. 2020 Dec [citado: 01/03/2024]; 5(12): e621. Disponible en: https://revistamedicasinergia.com/index.php/rms/article/view/621

4. Saraf SL, Molokie RE, Nouraie M, Sable CA, Luchtman-Jones L, Ensing GJ, et al. Differences in the clinical and genotypic presentation of sickle cell disease around the world. Vol. 15, Paediatric Respiratory Reviews. [Internet]. 2015 [citado: 01/03/2024]; 15(1): 4–12. Disponible en: https://doi.org/10.1016/j.prrv.2013.11.003

5. Aghamolaei T, Pormehr-Yabandeh A, Hosseini Z, Roozbeh N, Arian M, Ghanbarnezhad A. Pregnancy in the Sickle Cell Disease and Fetomaternal Outcomes in Different Sickle cell Genotypes: A Systematic Review and Meta-Analysis. Ethiop J Health Sci. [Internet]. 2022 Jul [citado: 01/03/2024]; 32(4): 849–64. Disponible en: https://doi.org/10.4314/ejhs.v32i4.23

6. Jain D, Atmapoojya P, Colah R, Lodha P. Sickle cell disease and pregnancy. Mediterranean Journal of Hematology and Infectious Diseases. Universita Cattolica del Sacro Cuore [Internet]. 2019 [citado: 01/03/2024]; 11(1): e2019040. Disponible en: https://doi.org/10.4084/mjhid.2019.040

7. Martínez-Sánchez LM, Villegas-Alzate JD, Herrera-Almanza L, Correa-Saavedra MA, Gálvez-Cárdenas KM, Hernández-Martínez A, et al. Characterization of patients with sickle cell anemia in Medellin, Colombia. Medicina Interna de Mexico. [Internet]. 2022 Sep [citado: 01/03/2024]; 38(5): 1012–8. Disponible en: https://www.medigraphic.com/pdfs/medintmex/mim-2022/mim225e.pdf

8. Quiñonez Lugo MC. Estilos de vida en personas con anemia drepanocítica en el Cantón San Lorenzo [Tesis] Pontificia Universidad Católica del Ecuador[Internet]; 2017[citado: 01/03/2024]. Disponible en: https://repositorio.puce.edu.ec/handle/123456789/37064

9. Sousa VT de, Ballas SK, Leite JM, Olivato MCA, Cancado RD. Maternal and perinatal outcomes in pregnant women with sickle cell disease: an update. Hematol Transfus Cell Ther [Internet]. 2022 [citado: 01/03/2024]; 44(3): 369-73. Disponible en: http://dx.doi.org/10.1016/j.htct.2020.12.009

10. Adesina OO, Brunson A, Fisch SC, Yu B, Mahajan A, Willen SM, Keegan THM, Wun T. Pregnancy outcomes in women with sickle cell disease in California. Am J Hematol. [Internet]. 2023 Mar [citado: 01/03/2024]; 98(3): 440-448. Disponible en: http://dx.doi.org/10.1002/ajh.26818

11. Lewis G, Thame M, Howitt C, Hambleton I, Serjeant GR. Pregnancy outcome in homozygous sickle cell disease: observations from the Jamaican Birth Cohort. BJOG [Internet]. 2021 [citado: 01/03/2024]; 128(10): 1703-10. Disponible en: http://dx.doi.org/10.1111/1471-0528.16696

12. Habibi A, Cannas G, Bartolucci P, Voskaridou E, Joseph L, Bernit E, et al. Outcomes of Pregnancy in Sickle Cell Disease Patients: Results from the Prospective ESCORT-HU Cohort Study. Biomedicines [Internet]. 2023 [citado: 01/03/2024]; 11: 597. Disponible en: https://doi.org/10.3390/biomedicines11020597

13. Prado-Molina DG, SernaTrejos JS, Quijano-Navarrete M. Primera terapia por edición génica en anemia de células falciformes: dilemas bioéticos. Rev Hisp Cienc Salud. [Internet]. 2024; [citado: 01/03/2024]; 10(1): 53-54. Disponible en: https://doi.org/10.56239/rhcs.2024.101.717

14. Olivo-Yepez A, Linares-Márquez P, Delgado-Enciso I, Morales-Romero Z. La terapia génica en México y España, una aproximación bioética desde la investigación científica. Rev. Bioética y Derecho [Internet]. 2021 [citado: 01/03/2024]; (53): 117-138. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1886-58872021000300007&lng=es

15. Lucero Flores KG, Reyes Rosero EA. Terapias génicas para tratar a pacientes con anemia de células falciformes. Revisión de literatura. Cienc. educ. (Holguin) [Internet]. 5 de abril de 2025 [citado: 15/04/2024]; 291-301. Disponible en: https://cienciayeducacion.com/index.php/journal/article/view/zenodo.15178002

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S1): e6862

16. Duque EL, Saavedra VME, Vergara YD, et al. Anemia de células falciformes en medicina de urgencias: una revisión basada en la evidencia. Med Int Mex. [Internet]. 2024 [citado: 01/03/2024]; 40(09): 581-590. Disponible en: https://www.medigraphic.com/pdfs/medintmex/mim-2024/mim249d.pdf

17. Shah N, Bhor M, Xie L, Paulose J, et al. Sickle cell disease complications: Prevalence and resource utilization. PLoS One [Internet]. 2019 [citado: 01/03/2024]; 14(7): e0214355. Disponible en: https://doi.org/10.1371/journal.pone.0214355

18. Hequet O, Fort R, Driss F. Red blood cell exchange in an emergency in sickle cell disease. Transfus Apher Sci [Internet]. 2020 [citado: 01/03/2024]; 59(6): 102996. Disponible en: https://doi.org/10.1016/j.transci.2020.102996

19. Ramsay Z, Bartlett R, Ali A, Grant J, et al. Sickle Cell Disease and Pain: Is it all Vaso-occlusive Crises? Clin J Pain [Internet]. 2021 [citado: 01/03/2024]; 37(8): 583-90. Disponible en: https://doi.org/10.1097/AJP.0000000000000949

20. Gaitán-Lee H, Chacón-Cas-tillo CL, Stangl-Correa WP, Stangl-Herera WP, Alzate-Chacón RI, Gómez-Menéndez JM, et al. Protocolo multidisciplinario para el manejo de pacientes con anemia de células falciformes llevados a artro-plastia total de cadera. Experiencia en un hospital de Cali, Colombia. Rev Col Or Tra. [Internet]. 2024 [citado: 01/03/2024]; 38(2): e97. Disponible en: https://doi.org/10.58814/01208845.97

21. Piel FB, Rees DC, DeBaun MR, Nnodu O, Ranque B, Thompson AA, et al. Defining global strategies to improve outcomes in sickle cell disease: a Lancet Haematology Commission. Lancet Haematol. [Internet]. 2023 [citado: 01/03/2024]; 10(8): e633-e686. Disponible en: https://pubmed.ncbi.nlm.nih.gov/37451304/

22. Morón Serrano SJ, Giraldo Cuartas CE, Ariza Parra EJ, Gaviria Jaramillo LM, Hernández Rodríguez JC, Cárdenas Ramos RM, et al. Indicaciones y complicaciones del soporte transfusional en pacientes con enfermedad de células falciformes. Acta Médica Colombiana [Internet]. 2025 [citado: 08/02/2025]; 50(2). Disponible en: https://doi.org/10.36104/amc.2025.3785

23. Rollins MR, Chou ST. Adverse events of red blood cell transfusions in patients with sickle cell disease. Transfus Apher Sci. [Internet]. 2022 [citado: 08/02/2025]; 61(5): 103557. Disponible en: https://pubmed.ncbi.nlm.nih.gov/36064527/

24. Ackfeld T, Schmutz T, Guechi Y, Le Terrier C. Blood Transfusion Reactions—A Comprehensive Review of the Literature including a Swiss Perspective. J Clin Med. [Internet]. 2022 [citado: 08/02/2025]; 11(10): 2859. Disponible en: https://pubmed.ncbi.nlm.nih.gov/35628985/