Elite Journal of Haematology. Volume 2 issue 3(2024), Pp. 81-95
https://epjournals.com/journals/EJH

Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology

*Emmanuel Ifeanyi Obeagu

Department of Medical Laboratory Science, Kampala International University, Uganda.

*Corresponding authour: Emmanuel Ifeanyi Obeagu, Department of Medical Laboratory Science, Kampala International University, Uganda, emmanuelobeagu@yahoo.com, ORCID: 0000-0002-4538-0161

Abstract

Sickle Cell Anemia (SCA), a hereditary hemoglobinopathy, is characterized by distorted red blood cells leading to vaso-occlusive complications and chronic hemolytic anemia. While the genetic basis of SCA is well-established, emerging research points to environmental factors as potential modulators of disease severity. Among these factors, Chromium VI, a known toxic heavy metal, has been implicated as a silent aggressor influencing the pathophysiology of SCA. This in-depth review critically examines the intricate interplay between Chromium VI exposure and the molecular processes underlying SCA. Exploration of sources and bioavailability of Chromium VI precedes a detailed analysis of its impact on molecular mechanisms within the context of SCA. Oxidative stress, hemoglobin interaction, inflammatory pathways, and epigenetic effects are scrutinized to elucidate the potential pathways through which Chromium VI exacerbates the manifestations of SCA. Clinical consequences of Chromium VI exposure in SCA patients are explored, shedding light on the exacerbation of symptoms, disease progression, and complications. The review further investigates genetic susceptibility, emphasizing polymorphisms and individual variability in Chromium VI metabolism. Diagnostic challenges arising from overlapping symptoms and potential biomarkers are discussed, offering insights into the complexity of identifying Chromium VI impact in SCA patients. The therapeutic implications of mitigating Chromium VI exposure in the management of SCA are presented, offering a perspective on environmental interventions to improve patient outcomes. Through a meticulous examination of the literature, this review endeavors to stimulate further inquiry and inform strategies for mitigating the impact of Chromium VI on individuals with Sickle Cell Anemia.

Keywords*: sickle cell anemia, Chromium VI, inflammation, vaso-occlusiove crisis, pathophysiology*

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

Introduction

Sickle Cell Anemia (SCA), a hereditary hemoglobinopathy, stands as a formidable global health challenge, affecting millions of individuals worldwide.[1] This genetic disorder, characterized by the abnormal sickling of red blood cells, leads to vaso-occlusive crises, chronic anemia, and a myriad of complications that significantly impact the quality of life for those afflicted.[2] While the genetic underpinnings of SCA are well-established, recent investigations have turned attention towards the potential influence of environmental factors in shaping the clinical course of the disease.[3] Among the myriad environmental variables, heavy metal exposure has emerged as a focus of interest, with Chromium VI, a known toxic metal, being implicated in the exacerbation of SCA pathophysiology.[4] This paper aims to scrutinize the complex interplay between Chromium VI and the molecular processes that govern SCA, shedding light on the potential role of this silent aggressor in modulating disease severity.

This paper is guided by the overarching question: Could Chromium VI, a heavy metal ubiquitous in various industrial processes and environmental settings, be an underrecognized contributor to the intricate tapestry of SCA pathophysiology? The subsequent sections will systematically unravel the evidence, starting with the sources and bioavailability of Chromium VI, before delving into its molecular impact on oxidative stress, hemoglobin stability, inflammatory pathways, and epigenetic modifications within the unique physiological milieu of SCA.

Chromium VI Exposure in Sickle Cell Anemia

Chromium VI exposure in individuals with Sickle Cell Anemia (SCA) represents an area of increasing concern, as it adds a potential environmental dimension to the complex interplay of genetic and external factors influencing the severity and progression of the disease.[5] Chromium VI, a toxic heavy metal, is encountered in various industrial processes, including metal plating, leather tanning, and stainless-steel production, as well as in environmental settings such as water sources contaminated by industrial discharges.[6] Individuals with SCA, often subjected to regular medical treatments and monitoring, may encounter Chromium VI in healthcare settings where chrome-containing medical instruments and devices are used.[7] Residences and communities near industrial facilities that release Chromium VI into the air, water, or soil may expose SCA patients to elevated levels of this toxic metal.[8] Certain foods, especially those grown in contaminated areas, may contain traces of Chromium VI. Understanding the dietary habits of individuals with SCA is crucial in assessing potential exposure.[9] Some medications and supplements may inadvertently expose SCA patients to Chromium VI, particularly if these products are not rigorously regulated or monitored.10 SCA patients may exhibit altered metabolism and clearance mechanisms, potentially affecting the way Chromium VI is absorbed, distributed, metabolized, and excreted.[11] The chronic inflammatory state and oxidative stress characteristic of SCA may render individuals more susceptible to the toxic effects of Chromium VI, exacerbating existing health challenges.[12]

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

Clinical Evidence of Chromium VI Impact on SCA Severity

Studies suggest that Chromium VI exposure may contribute to the exacerbation of SCA symptoms, including increased frequency and intensity of vaso-occlusive crises.[13] Chromium VI may interact with red blood cells, influencing hemoglobin stability and potentially aggravating the chronic hemolytic anemia characteristic of SCA.[14] There is a need for rigorous clinical investigations to ascertain the impact of Chromium VI exposure on complications associated with SCA, such as pulmonary hypertension, organ damage, and increased susceptibility to infections.[15] Understanding the sources, bioavailability, and clinical consequences of Chromium VI exposure in individuals with Sickle Cell Anemia is paramount for developing targeted interventions, mitigating environmental risks, and improving the overall management and well-being of SCA patients. Further research is essential to establish clear associations and unravel the underlying mechanisms of Chromium VI's influence on the pathophysiology of Sickle Cell Anemia.

Molecular Mechanisms

Investigating the molecular mechanisms by which Chromium VI influences the pathophysiology of Sickle Cell Anemia (SCA) reveals a complex interplay between the toxic effects of the metal and the underlying genetic and physiological factors inherent to the disease.[16] Chromium VI is known to undergo redox cycling, leading to the generation of reactive oxygen species (ROS), including free radicals and hydrogen peroxide.[17] Elevated ROS levels contribute to oxidative stress, a phenomenon already heightened in SCA due to the abnormal hemoglobin and chronic inflammation.[18] SCA patients, with their inherently fragile red blood cells, may be more susceptible to the oxidative damage induced by Chromium VI, potentially exacerbating hemolysis and vaso-occlusive crises.[19]

Interaction with Hemoglobin S and Red Blood Cells

Chromium VI may interact with hemoglobin S, inducing structural changes that compromise its stability and function. Altered hemoglobin function can contribute to the characteristic sickling of red blood cells in SCA, leading to vaso-occlusive events.[20] Chromium VI may influence the integrity of the red blood cell membrane, impacting its deformability and rheological properties. These alterations could contribute to the adhesion of sickled cells to the vascular endothelium, exacerbating the vaso-occlusive processes.[21] Chromium VI exposure may activate inflammatory pathways, amplifying the chronic inflammatory state inherent to SCA. Increased inflammation can contribute to the activation of leukocytes and endothelial cells, further promoting vaso-occlusion.[22] Chromium VI-induced endothelial dysfunction may exacerbate the adhesive interactions between sickled red blood cells and the vascular endothelium. Impaired endothelial function contributes to the development of vascular complications in SCA, including pulmonary hypertension and organ damage.[23] Chromium VI is known to induce DNA damage, potentially affecting the already compromised repair mechanisms in SCA. Increased genomic instability may contribute to the

progression of the disease and influence the severity of clinical manifestations. Chromium VI exposure may induce epigenetic modifications, altering gene expression patterns. Epigenetic changes could impact the regulation of genes involved in SCA pathophysiology, influencing disease outcomes.[24]

Understanding these molecular mechanisms provides a foundation for exploring the nuanced ways in which Chromium VI may act as a silent aggressor in SCA pathophysiology. It underscores the importance of elucidating the specific pathways through which environmental factors interact with the genetic basis of SCA, potentially offering new avenues for therapeutic interventions and environmental management strategies. Further research is imperative to validate these mechanisms and translate findings into targeted approaches for mitigating the impact of Chromium VI on individuals with Sickle Cell Anemia.

Clinical Consequences

The clinical consequences of Chromium VI exposure in individuals with Sickle Cell Anemia (SCA) are multifaceted, potentially influencing the severity of the disease and exacerbating its complications.[25] Chromium VI exposure may contribute to the exacerbation of vaso-occlusive crises, a hallmark feature of SCA.[26] The toxic effects of Chromium VI on red blood cells and vascular function could further amplify the frequency and severity of painful episodes.[27] Chromium VI-induced hemolysis and oxidative stress may exacerbate the chronic hemolytic anemia characteristic of SCA. This can lead to increased fatigue, pallor, and a higher demand for transfusions in affected individuals. Chromium VI interactions with hemoglobin S may compromise its stability, potentially influencing the kinetics of sickling and desickling.[28] Altered hemoglobin function could contribute to the abnormal behavior of red blood cells and worsen the clinical course of SCA.[29] Chromium VI-induced oxidative stress may intensify hemolysis, leading to the release of free hemoglobin and other hemolytic byproducts. This process could contribute to increased organ damage and complications associated with SCA. Chromium VI exposure may exacerbate endothelial dysfunction, potentially contributing to the development and progression of pulmonary hypertension in SCA.[30] Pulmonary complications are significant contributors to morbidity and mortality in SCA patients.[31] Chronic exposure to Chromium VI may contribute to organ damage, particularly in organs vulnerable to hemodynamic changes and vascular complications. The kidneys, liver, and spleen may be particularly susceptible to the combined effects of SCA and Chromium VI toxicity.[32] Chromium VI-induced immunomodulation may compromise the immune system in SCA patients, increasing their vulnerability to infections. Infections can further complicate the clinical course and contribute to acute complications. Exacerbation of symptoms, increased frequency of crises, and additional complications may collectively reduce the overall quality of life for individuals with SCA exposed to Chromium VI.[33] Chronic exposure to Chromium VI may contribute to long-term morbidity, potentially influencing the overall life expectancy of individuals with SCA.[34] The cumulative impact of environmental

factors on disease outcomes underscores the need for comprehensive care and intervention strategies.

Diagnostic Challenges

The clinical consequences of Chromium VI exposure may overlap with the symptoms of SCA, posing challenges in differentiating the specific contributions of environmental factors to disease manifestations. Precise diagnostic tools are needed to identify Chromium VI impact amidst the complex clinical presentation of SCA.[35] Understanding the clinical consequences of Chromium VI exposure in Sickle Cell Anemia is critical for developing targeted interventions, informing patient care strategies, and highlighting the importance of environmental management in the holistic approach to managing this complex genetic disorder. Ongoing research is essential to further elucidate the specific interactions and outcomes associated with Chromium VI exposure in individuals with SCA.

Genetic Susceptibility and Interindividual Variability

Genetic susceptibility and interindividual variability play crucial roles in shaping the impact of Chromium VI exposure on individuals with Sickle Cell Anemia (SCA). The intricate interplay between the genetic background of SCA patients and their response to environmental toxins like Chromium VI contributes to variations in susceptibility, toxicity, and clinical outcomes.[36] Genetic polymorphisms in enzymes involved in Chromium VI metabolism, such as those in the glutathione S-transferase (GST) family, may influence an individual's ability to detoxify and eliminate the metal. Variations in DNA repair pathways, including genes involved in base excision repair and homologous recombination, may influence the response to Chromium VI-induced DNA damage. Genetic variations in genes regulating oxidative stress responses, such as superoxide dismutase (SOD) and catalase, may impact an individual's susceptibility to Chromium VI-induced oxidative damage.[36]

Interindividual differences in the absorption and distribution of Chromium VI may be influenced by genetic factors governing the expression of transport proteins and metal-binding molecules. Genetic variations in Phase I and Phase II biotransformation enzymes, including cytochrome P450 enzymes and conjugation enzymes, can affect the metabolism of Chromium VI. Genetic factors influencing renal function and excretion pathways may contribute to variability in Chromium VI elimination rates.[37] Gene-environment interactions, where specific genetic profiles interact with environmental exposures, may result in synergistic effects, either amplifying or attenuating the toxic impact of Chromium VI in SCA patients. Epigenetic modifications, such as DNA methylation and histone acetylation, can be influenced by genetic factors and may further modulate the response to Chromium VI exposure.[36]

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

SCA encompasses a spectrum of genotypes, and variations in the severity of the disease may contribute to differences in susceptibility to environmental toxins like Chromium VI. Genetic modifiers of SCA, such as variations in fetal hemoglobin levels and other modifying genes, may influence the overall impact of Chromium VI exposure on disease severity.[38] Understanding the genetic susceptibility and interindividual variability in Chromium VI metabolism and response is pivotal for personalized medicine approaches in managing individuals with Sickle Cell Anemia. Tailoring interventions based on an individual's genetic makeup can enhance the precision and efficacy of environmental management strategies, mitigating the impact of Chromium VI on SCA patients. Ongoing research in this area is essential for uncovering specific genetic markers and elucidating the complex gene-environment interactions that underlie the variability in responses to Chromium VI in the context of SCA.

Therapeutic Implications

The therapeutic implications of addressing Chromium VI exposure in individuals with Sickle Cell Anemia (SCA) are multifaceted, encompassing environmental management strategies, targeted medical interventions, and comprehensive patient care. Tailoring therapeutic approaches to mitigate the impact of Chromium VI in the context of SCA requires a holistic and interdisciplinary perspective. [39] Implementing measures to reduce occupational and residential exposure to Chromium VI is crucial.[40] This includes the use of personal protective equipment in occupational settings and identification and remediation of contaminated environments. Ensuring the safety of water sources and monitoring food supplies for Chromium VI contamination is essential. Collaborating with environmental agencies to regulate and monitor industrial discharges is a critical component of environmental management. SCA patients with potential Chromium VI exposure should undergo regular health assessments, including monitoring of hematological parameters, liver and kidney function, and markers of oxidative stress.[41] Research efforts should focus on the development of specific biomarkers for Chromium VI exposure in SCA patients to facilitate early detection and intervention. Considering the role of oxidative stress in both SCA and Chromium VI toxicity, antioxidant supplementation may be explored as a therapeutic intervention to mitigate oxidative damage.[42] Anti-inflammatory agents may be considered to modulate the inflammatory pathways activated by both SCA and Chromium VI exposure, potentially reducing complications associated with chronic inflammation.[43] Tailoring treatment plans based on the specific genotype and phenotype of the SCA patient is crucial. Genetic factors influencing susceptibility to Chromium VI may guide individualized therapeutic approaches. Addressing coexisting health conditions and comorbidities is integral to comprehensive care. Therapeutic strategies should consider potential interactions between SCA, Chromium VI exposure, and other health challenges.[44] Patient education plays a pivotal role in raising awareness about environmental risks and advocating for protective measures.[45] Empowering individuals with SCA to actively participate in their healthcare can lead to better outcomes. Engaging communities in educational initiatives and advocacy efforts enhances collective awareness and encourages proactive measures to reduce environmental risks.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

Continued research into novel therapies that specifically target the intersection of Chromium VI exposure and SCA pathophysiology is essential.[46] Clinical trials exploring the efficacy of targeted interventions are warranted. Long-term studies assessing the impact of environmental management strategies and therapeutic interventions on the health outcomes of individuals with SCA and Chromium VI exposure are needed[47]. Advocating for and contributing to the development of stringent environmental regulations and workplace safety standards is crucial for preventing Chromium VI exposure. Collaboration between healthcare professionals and policymakers is essential to integrate health considerations into environmental and occupational regulations, ensuring the protection of vulnerable populations. Adopting a multidisciplinary approach to patient care, involving hematologists, environmental scientists, toxicologists, and public health professionals, facilitates a holistic understanding and management of the complex interplay between SCA and Chromium VI exposure.[48] Addressing Chromium VI exposure in the context of Sickle Cell Anemia requires a comprehensive and integrated approach, ranging from environmental interventions to personalized medical care.[49] Continued collaboration between healthcare practitioners, researchers, policymakers, and community stakeholders is essential to develop effective therapeutic strategies and improve the overall well-being of individuals with SCA affected by environmental factors.

Future Directions and Research Gaps

As research at the intersection of Chromium VI exposure and Sickle Cell Anemia (SCA) pathophysiology progresses, several future directions and research gaps emerge, calling for focused investigations to advance our understanding and improve patient outcomes.[50] Further elucidating the molecular interactions between Chromium VI and the genetic and physiological factors in SCA patients is essential. This includes in-depth studies on the specific pathways through which Chromium VI modulates oxidative stress, hemoglobin stability, and inflammatory responses. Identifying genetic modifiers that influence individual susceptibility to Chromium VI toxicity in the context of SCA is crucial. Investigating specific polymorphisms and their impact on disease severity will enhance our ability to tailor interventions. Developing highly specific biomarkers for Chromium VI exposure in individuals with SCA is a priority.[51] Such biomarkers will aid in accurate diagnosis, monitoring, and assessment of the impact of environmental exposure on disease progression. Establishing comprehensive biomarker panels that reflect both SCA-specific and Chromium VI-induced effects will contribute to a more nuanced understanding of the combined impact of genetic and environmental factors.

Conducting longitudinal studies to assess the long-term health outcomes of individuals with SCA exposed to Chromium VI is crucial.[52] These studies should evaluate the cumulative impact on morbidity, mortality, and overall quality of life. Implementing robust methods for tracking environmental exposure over time will facilitate the establishment of clear correlations between Chromium VI exposure levels and disease progression in SCA. Conducting comprehensive analyses of gene-environment interactions is necessary. Understanding how specific genetic

profiles modulate the response to Chromium VI exposure in individuals with SCA will inform targeted therapeutic strategies. Investigating the role of epigenetic modifications in mediating the effects of Chromium VI exposure in SCA patients is an important avenue for research. This includes exploring changes in DNA methylation patterns and histone modifications.

Developing targeted therapeutic interventions that specifically address the combined effects of Chromium VI exposure and SCA is essential.[53] Investigating the efficacy of anti-oxidative agents and anti-inflammatory drugs in mitigating the impact of environmental factors is warranted. Exploring the feasibility of individualized treatment plans based on both genetic and environmental factors will contribute to precision medicine approaches in managing individuals with SCA exposed to Chromium VI. Integrating patient-reported outcomes into research designs will provide valuable insights into the subjective experiences of individuals with SCA and Chromium VI exposure. This patient-centric approach is crucial for developing interventions that align with patient needs and priorities. Investigating the psychosocial impacts of Chromium VI exposure in SCA patients, including factors such as mental health, social support, and quality of life, is an area that merits attention. Collaborating with policymakers to integrate health considerations into environmental regulations and occupational safety standards is imperative.[54] This collaboration will contribute to preventing Chromium VI exposure and protecting vulnerable populations. Developing public health initiatives that raise awareness about environmental risks and promote protective measures among individuals with SCA is essential. Community engagement strategies can enhance the success of these initiatives. Addressing these research gaps will not only advance our understanding of the complex interplay between Chromium VI exposure and Sickle Cell Anemia but also contribute to the development of targeted interventions and improved clinical management. Ongoing collaboration between researchers, clinicians, environmental scientists, and policymakers is vital to drive progress in these future directions.[54-92]

Conclusion

In conclusion, the intersection of Chromium VI exposure and Sickle Cell Anemia (SCA) pathophysiology represents a complex and emerging field that demands thorough investigation. SCA, a hereditary hemoglobinopathy, is intricately linked with both genetic predispositions and environmental factors. The introduction of Chromium VI as a potential environmental contributor adds layers of complexity to the understanding of disease manifestations.

References

1. Mirghani HO, Alatawi NM, Alenzi MT, Alatawi NS, Alsabeelah NM, Almutairi MF, Alshammari AM, Alomrani MN, Alrubayyi WS, Alfarshoti AM, Alenzi BM. Association between Sickle Cell Anemia and Malaria: A Systematic Review of Previous Literature: Sickle Cell Anemia and Malaria: A Systematic Review. Saudi Medical Horizons Journal. 2023;3(3):118-30.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

2. Osunkwo I, Manwani D, Kanter J. Current and novel therapies for the prevention of vaso-occlusive crisis in sickle cell disease. Therapeutic Advances in Hematology. 2020:2040620720955000.
3. Snyder-Mackler N, Burger JR, Gaydosh L, Belsky DW, Noppert GA, Campos FA, Bartolomucci A, Yang YC, Aiello AE, O'Rand A, Harris KM. Social determinants of health and survival in humans and other animals. Science. 2020;368(6493): eaax9553.
4. Rahman I, Bagchi D, editors. Inflammation, advancing age and nutrition: research and clinical interventions. Academic Press; 2013.
5. Alapan Y, Fraiwan A, Kucukal E, Hasan MN, Ung R, Kim M, Odame I, Little JA, Gurkan UA. Emerging point-of-care technologies for sickle cell disease screening and monitoring. Expert review of medical devices. 2016;13(12):1073-93.
6. Kumar V, Dwivedi SK. A review on accessible techniques for removal of hexavalent Chromium and divalent Nickel from industrial wastewater: Recent research and future outlook. Journal of Cleaner Production. 2021; 295:126229.
7. Nur-E-Alam M, Mia MA, Ahmad F, Rahman MM. An overview of chromium removal techniques from tannery effluent. Applied Water Science. 2020;10(9):205.
8. Islam MS, Ismail Z, Jamal MH, Ibrahim Z, Jumain M, Islam AR, Kabir MH, Asraful Islam SM, Ahmed S, Phoungthong K, Ibrahim KA. Heavy metals from different land use soil in the capital of ancient Pundranagar, Bangladesh: a preliminary study for ecological risk assessment. Chemistry and Ecology. 2022;38(8):720-43.
9. Andrade-Rivas F, Afshari R, Yassi A, Mardani A, Taft S, Guttmann M, Rao AS, Thomas S, Takaro T, Spiegel JM. Industrialization and food safety for the Tsleil-Waututh Nation: An analysis of chemical levels in shellfish in Burrard Inlet. Environmental Research. 2022; 206:112575.
10. Telen MJ, Malik P, Vercellotti GM. Therapeutic strategies for sickle cell disease: towards a multi-agent approach. Nature reviews Drug discovery. 2019;18(2):139-58.
11. Bhaskar M, Telessy IG, Buttar HS. The Importance of Drug Dose Adjustment in Elderly Patients with Special Considerations for Patients on Diverse Co-medications and Antidepressants. Biomedical Translational Research: Drug Design and Discovery. 2022:231-72.
12. Khan SA, Damanhouri G, Ali A, Khan SA, Khan A, Bakillah A, Marouf S, Al Harbi G, Halawani SH, Makki A. Precipitating factors and targeted therapies in combating the perils of sickle cell disease---A special nutritional consideration. Nutrition & metabolism. 2016;13(1):1-2.
13. Ballas SK, Kesen MR, Goldberg MF, Lutty GA, Dampier C, Osunkwo I, Wang WC, Hoppe C, Hagar W, Darbari DS, Malik P. Beyond the definitions of the phenotypic complications of sickle cell disease: an update on management. The Scientific World Journal. 2012.
14. de Paula CP, de Oliveira da Silva JP, Romanello KS, Bernardo VS, Torres FF, da Silva DG, da Cunha AF. Peroxiredoxins in erythrocytes: far beyond the antioxidant role. Journal of Molecular Medicine. 2023:1-9.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

15. Hebbel RP. Reconstructing sickle cell disease: a data-based analysis of the "hyperhemolysis paradigm" for pulmonary hypertension from the perspective of evidence-based medicine. American journal of hematology. 2011;86(2):123-54.
16. Tampaki A, Gavriilaki E, Varelas C, Anagnostopoulos A, Vlachaki E. Complement in sickle cell disease and targeted therapy: I know one thing, that I know nothing. Blood Reviews. 2021; 48:100805.
17. Hu G, Zheng P, Feng H, Jia G. Imbalance of oxidative and reductive species involved in chromium (VI)-induced toxic effects. React. Oxyg. Species. 2017;3(11).
18. Vona R, Sposi NM, Mattia L, Gambardella L, Straface E, Pietraforte D. Sickle cell disease: role of oxidative stress and antioxidant therapy. Antioxidants. 2021;10(2):296.
19. Ahmed SG, Ibrahim UA. A compendium of pathophysiologic basis of etiologic risk factors for painful vaso-occlusive crisis in sickle cell disease. Nigerian Journal of Basic and Clinical Sciences. 2017;14(2):57-77.
20. Wise SS, Holmes AL, Wise, Sr. JP. Hexavalent chromium-induced DNA damage and repair mechanisms. Reviews on environmental health. 2008;23(1):39-58.
21. Dugmonits KN, Chakraborty P, Hollandi R, Zahorán S, Pankotai-Bodó G, Horváth P, Orvos H, Hermesz E. Maternal Smoking Highly Affects the Function, Membrane Integrity, and Rheological Properties in Fetal Red Blood Cells. Oxidative Medicine and Cellular Longevity. 2019.
22. Zimmermann HW, Trautwein C, Tacke F. Functional role of monocytes and macrophages for the inflammatory response in acute liver injury. Frontiers in physiology. 2012; 3:56.
23. Sun X, Ku DD. Selective right, but not left, coronary endothelial dysfunction precedes development of pulmonary hypertension and right heart hypertrophy in rats. American Journal of Physiology-Heart and Circulatory Physiology. 2006;290(2):H758-64.
24. Ray PD, Yosim A, Fry RC. Incorporating epigenetic data into the risk assessment process for the toxic metals arsenic, cadmium, chromium, lead, and mercury: strategies and challenges. Frontiers in genetics. 2014; 5:201.
25. Alabi OJ, Adegboyega FN, Olawoyin DS, Babatunde OA. Functional foods: promising therapeutics for Nigerian Children with sickle cell diseases. Heliyon. 2022.
26. Lamarre Y, Nader E, Connes P, Romana M, Garnier Y. Extracellular vesicles in sickle cell disease: a promising tool. Bioengineering. 2022;9(9):439.
27. Darbari DS, Onyekwere O, Nouraie M, Minniti CP, Luchtman-Jones L, Rana S, Sable C, Ensing G, Dham N, Campbell A, Arteta M. Markers of severe vaso-occlusive painful episode frequency in children and adolescents with sickle cell anemia. The Journal of pediatrics. 2012;160(2):286-90.
28. Jana S, Strader MB, Meng F, Hicks W, Kassa T, Tarandovskiy I, De Paoli S, Simak J, Heaven MR, Belcher JD, Vercellotti GM. Hemoglobin oxidation–dependent reactions promote interactions with band 3 and oxidative changes in sickle cell–derived microparticles. JCI insight. 2018;3(21).
29. Hebbel RP, Belcher JD, Vercellotti GM. The multifaceted role of ischemia/reperfusion in sickle cell anemia. The Journal of Clinical Investigation. 2020;130(3):1062-72.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

30. Hoppe CC. Inflammatory mediators of endothelial injury in sickle cell disease. Hematology/Oncology Clinics. 2014;28(2):265-86.
31. Fitzhugh CD, Lauder N, Jonassaint JC, Telen MJ, Zhao X, Wright EC, Gilliam FR, De Castro LM. Cardiopulmonary complications leading to premature deaths in adult patients with sickle cell disease. American journal of hematology. 2010;85(1):36-40.
32. Pfohl-Leszkowicz A, Manderville RA. Ochratoxin A: An overview on toxicity and carcinogenicity in animals and humans. Molecular nutrition & food research. 2007;51(1):61-99.
33. McGann PT, Nero AC, Ware RE. Clinical features of β-thalassemia and sickle cell disease. Gene and Cell Therapies for Beta-Globinopathies. 2017:1-26.
34. Schaefer BA, Flanagan JM, Alvarez OA, Nelson SC, Aygun B, Nottage KA, George A, Roberts CW, Piccone CM, Howard TA, Davis BR. Genetic modifiers of white blood cell count, albuminuria and glomerular filtration rate in children with sickle cell anemia. PloS one. 2016;11(10): e0164364.
35. Poon A, Zhang Y, Chandrasekaran A, Phanthong P, Schmid B, Nielsen TT, Freude KK. Modeling neurodegenerative diseases with patient-derived induced pluripotent cells: Possibilities and challenges. New biotechnology. 2017; 39:190-8.
36. Perera FP. Molecular epidemiology: insights into cancer susceptibility, risk assessment, and prevention. JNCI: Journal of the National Cancer Institute. 1996;88(8):496-509.
37. Gundacker C, Gencik M, Hengstschläger M. The relevance of the individual genetic background for the toxicokinetics of two significant neurodevelopmental toxicants: mercury and lead. Mutation Research/Reviews in Mutation Research. 2010 Oct 1;705(2):130-40.
38. Ilesanmi OO. Pathological basis of symptoms and crises in sickle cell disorder: implications for counseling and psychotherapy. Hematology reports. 2010;2(1): e2.
39. Madigan C, Malik P. Pathophysiology and therapy for haemoglobinopathies; Part I: sickle cell disease. Expert reviews in molecular medicine. 2006;8(9):1-23.
40. Kimbrough DE, Cohen Y, Winer AM, Creelman L, Mabuni C. A critical assessment of chromium in the environment. Critical reviews in environmental science and technology. 1999;29(1):1-46.
41. Kerchberger VE, Ware LB. The role of circulating cell-free hemoglobin in sepsis-associated acute kidney injury. InSeminars in nephrology, 2020; 40 (2):148-159.
42. Al-Naama LM, Hassan MA, Mehdi JK. Association of erythrocytes antioxidant enzymes and their cofactors with markers of oxidative stress in patients with sickle cell anemia. Qatar Medical Journal. 2015;2015(2):14.
43. Bendotti G, Montefusco L, Lunati ME, Usuelli V, Pastore I, Lazzaroni E, Assi E, Seelam AJ, El Essawy B, Jang J, Loretelli C. The anti-inflammatory and immunological properties of GLP-1 Receptor Agonists. Pharmacological Research. 2022; 182:106320.
44. Empana JP, Blom MT, Böttiger BW, Dagres N, Dekker JM, Gislason G, Jouven X, Meitinger T, Ristagno G, Schwartz PJ, Jonsson M. Determinants of occurrence and

survival after sudden cardiac arrest–a European perspective: the ESCAPE-NET project. Resuscitation. 2018; 124:7-13.
45. Castro EM, Van Regenmortel T, Vanhaecht K, Sermeus W, Van Hecke A. Patient empowerment, patient participation and patient-centeredness in hospital care: A concept analysis based on a literature review. Patient education and counseling. 2016 Dec 1;99(12):1923-39.
46. Pranzatelli MR. Advances in biomarker-guided therapy for pediatric-and adult-onset neuroinflammatory disorders: targeting chemokines/cytokines. Frontiers in Immunology. 2018; 9:557.
47. Leung AO. Environmental contamination and health effects due to E-waste recycling. Electronic waste management and treatment technology. 2019:335-62.
48. Maxwell R, O'Brien M, O'Donnell D, Christophers L, Kroll T. Using a multidisciplinary approach to reveal decision-making capacity within acute care for an individual with aphasia. SAGE Open Medical Case Reports. 2021; 9:2050313X211027098.
49. Telfer P, Kaya B. Optimizing the care model for an uncomplicated acute pain episode in sickle cell disease. Hematology 2014, the American Society of Hematology Education Program Book. 2017;2017(1):525-33.
50. Williams RA. Blacks in Medicine: Clinical, Demographic, and Socioeconomic Correlations. Springer Nature; 2020.
51. Goodman SR, Pace BS, Hansen KC, D'alessandro A, Xia Y, Daescu O, Glatt SJ. Minireview: Multiomic candidate biomarkers for clinical manifestations of sickle cell severity: Early steps to precision medicine. Experimental Biology and Medicine. 2016;241(7):772-81.
52. Irani F, Kalkstein S, Moberg EA, Moberg PJ. Neuropsychological performance in older patients with schizophrenia: a meta-analysis of cross-sectional and longitudinal studies. Schizophrenia bulletin. 2011;37(6):1318-26.
53. Velthorst E, Koeter M, Van Der Gaag M, Nieman DH, Fett AK, Smit F, Staring AB, Meijer C, De Haan L. Adapted cognitive–behavioural therapy required for targeting negative symptoms in schizophrenia: meta-analysis and meta-regression. Psychological medicine. 2015;45(3):453-65.
54. Loeppke RR, Hohn T, Baase C, Bunn WB, Burton WN, Eisenberg BS, Ennis T, Fabius R, Hawkins RJ, Hudson TW, Hymel PA. Integrating health and safety in the workplace: how closely aligning health and safety strategies can yield measurable benefits. Journal of Occupational and Environmental Medicine. 2015;57(5):585-97.
55. Obeagu EI, Ochei KC, Nwachukwu BN, Nchuma BO. Sickle cell anaemia: a review. Scholars Journal of Applied Medical Sciences. 2015;3(6B):224422-52.
56. Obeagu EI. Erythropoeitin in Sickle Cell Anaemia: A Review. International Journal of Research Studies in Medical and Health Sciences. 2020;5(2):22-28.
57. Obeagu EI. Sickle Cell Anaemia: Haemolysis and Anemia. Int. J. Curr. Res. Chem. Pharm. Sci. 2018;5(10):20-21.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

58. Obeagu EI, Muhimbura E, Kagenderezo BP, Uwakwe OS, Nakyeyune S, Obeagu GU. An Update on Interferon Gamma and C Reactive Proteins in Sickle Cell Anaemia Crisis. J Biomed Sci. 2022;11(10):84.
59. Obeagu EI, Bunu UO, Obeagu GU, Habimana JB. Antioxidants in the management of sickle cell anaemia: an area to be exploited for the wellbeing of the patients. International Research in Medical and Health Sciences. 2023 Sep 11;6(4):12-17.
60. Obeagu EI, Ogunnaya FU, Obeagu GU, Ndidi AC. Sickle cell anaemia: a gestational enigma. European Journal of Biomedical and Pharmaceutical Sciences. 2023;10((9): 72-75
61. Obeagu EI. An update on micro RNA in sickle cell disease. Int J Adv Res Biol Sci. 2018; 5:157-8.
62. Obeagu EI, Babar Q. Covid-19 and Sickle Cell Anemia: Susceptibility and Severity. J. Clinical and Laboratory Research. 2021;3(5):2768-0487.
63. Obeagu EI, Obeagu GU, Igwe MC, Alum EU, Ugwu OP. Men's Essential roles in the Management of Sickle Cell Anemia. **NEWPORT INTERNATIONAL JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 4(2):20-29**. https://doi.org/10.59298/NIJSES/2023/10.3.1111
64. Obeagu EI. Depression in Sickle Cell Anemia: An Overlooked Battle. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(10):41-.
65. Obeagu EI, Obeagu GU. Evaluation of Hematological Parameters of Sickle Cell Anemia Patients with Osteomyelitis in A Tertiary Hospital in Enugu, Nigeria. Journal of Clinical and Laboratory Research.2023;6(1):2768-0487.
66. Obeagu EI, Dahir FS, Francisca U, Vandu C, Obeagu GU. Hyperthyroidism in sickle cell anaemia. Int. J. Adv. Res. Biol. Sci. 2023;10(3):81-89.
67. Obeagu EI, Obeagu GU, Akinleye CA, Igwe MC. Nosocomial infections in sickle cell anemia patients: Prevention through multi-disciplinary approach: A review. Medicine. 2023;102(48):e36462.
68. Njar VE, Ogunnaya FU, Obeagu EI. Knowledge And Prevalence of The Sickle Cell Trait Among Undergraduate Students Of The University Of Calabar. Prevalence.;5(100):0-5.
69. Swem CA, Ukaejiofo EO, Obeagu EI, Eluke B. Expression of micro RNA 144 in sickle cell disease. Int. J. Curr. Res. Med. Sci. 2018;4(3):26-32.
70. Obeagu EI, Nimo OM, Bunu UO, Ugwu OP, Alum EU. Anaemia in children under five years: African perspectives. Int. J. Curr. Res. Biol. Med. 2023;1:1-7.
71. Obeagu EI. Sickle cell anaemia: Historical perspective, Pathophysiology and Clinical manifestations. Int. J. Curr. Res. Chem. Pharm. Sci. 2018;5(11):13-15.
72. Obeagu EI, Obeagu GU. Sickle Cell Anaemia in Pregnancy: A Review. International Research in Medical and Health Sciences. 2023 Jun 10;6(2):10-13.
73. Obeagu EI, Mohamod AH. An update on Iron deficiency anaemia among children with congenital heart disease. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(4):45-48.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

74. Edward U, Osuorji VC, Nnodim J, Obeagu EI. Evaluationof Trace Elements in Sickle Cell Anaemia Patients Attending Imo State Specialist Hospital, Owerri. Madonna University journal of Medicine and Health Sciences ISSN: 2814-3035. 2022 Mar 4;2(1):218-234.
75. Umar MI, Aliyu F, Abdullahi MI, Aliyu MN, Isyaku I, Aisha BB, Sadiq RU, Shariff MI, Obeagu EI. Assessment Of Factors Precipitating Sickle Cell Crises Among Under 5-Years Children Attending Sickle Cell Clinic Of Murtala Muhammad Specialist Hospital, Kano. blood.;11:16.
76. Obeagu EI. Vaso-occlusion and adhesion molecules in sickle cells disease. Int J Curr Res Med Sci. 2018;4(11):33-35.
77. Ifeanyi OE, Stella EI, Favour AA. Antioxidants In The Management of Sickle Cell Anaemia. Int J Hematol Blood Disord (Internet) 2018 (cited 2021 Mar 4); 3. Available from: https://symbiosisonlinepublishing. com/hematology/hema tology25. php. 2018 Sep.
78. Buhari HA, Ahmad AS, Obeagu EI. Current Advances in the Diagnosis and Treatment of Sickle Cell Anaemia. APPLIED SCIENCES (NIJBAS). 2023;4(1).
79. Nnodim J, Uche U, Ifeoma U, Chidozie N, Ifeanyi O, Oluchi AA. Hepcidin and erythropoietin level in sickle cell disease. British Journal of Medicine and Medical Research. 2015;8(3):261-5.
80. Obeagu EI. BURDEN OF CHRONIC OSTEOMYLITIS: REVIEW OF ASSOCIATIED FACTORS. Madonna University journal of Medicine and Health Sciences. 2023;3(1):1-6.
81. Aloh GS, Obeagu EI, Okoroiwu IL, Odo CE, Chibunna OM, Kanu SN, Elemchukwu Q, Okpara KE, Ugwu GU. Antioxidant-Mediated Heinz Bodies Levels of Sickle Erythrocytes under Drug-Induced Oxidative Stress. European Journal of Biomedical and Pharmaceutical sciences. 2015;2(1):502-507.
82. Obeagu EI, Malot S, Obeagu GU, Ugwu OP. HIV resistance in patients with Sickle Cell Anaemia. Newport International Journal of Scientific and Experimental Sciences (NIJSES). 2023;3(2):56-9.
83. Obeagu EI, Bot YS, Opoku D, Obeagu GU, Hassan AO. Sickle Cell Anaemia: Current Burden in Africa. International Journal of Innovative and Applied Research. 2023;11(2):12-14.
84. Obeagu EI, Obeagu GU. Sickle Cell Anaemia in Pregnancy: A Review. International Research in Medical and Health Sciences. 2023 Jun 10; 6 (2): 10-13.
85. Obeagu EI, Ogbuabor BN, Ikechukwu OA, Chude CN. Haematological parameters among sickle cell anemia patients' state and haemoglobin genotype AA individuals at Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. International Journal of Current Microbiology and Applied Sciences. 2014;3(3):1000-1005.
86. Ifeanyi OE, Nwakaego OB, Angela IO, Nwakaego CC. Haematological parameters among sickle cell anaemia... Emmanuel Ifeanyi1, et al. pdf• Obeagu. Int. J. Curr. Microbiol. App. Sci. 2014;3(3):1000-1005.
87. Obeagu EI, Abdirahman BF, Bunu UO, Obeagu GU. Obsterics characteristics that effect the newborn outcomes. Int. J. Adv. Res. Biol. Sci. 2023;10(3):134-143.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95

88. Obeagu EI, Opoku D, Obeagu GU. Burden of nutritional anaemia in Africa: A Review. Int. J. Adv. Res. Biol. Sci. 2023;10(2):160-163.
89. Ifeanyi E. Erythropoietin (Epo) Level in Sickle Cell Anaemia (HbSS) With Falciparum Malaria Infection in University Health Services, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. PARIPEX - INDIAN JOURNAL OF RESEARCH, 2015; 4(6): 258-259
90. Ifeanyi OE, Nwakaego OB, Angela IO, Nwakaego CC. Haematological parameters among sickle cell anaemia patients in steady state and haemoglobin genotype AA individuals at Michael Okpara, University of Agriculture, Umudike, Abia State, Nigeria. Int. J. Curr. Microbiol. App. Sci. 2014;3(3):1000-1005.
91. Ifeanyi OE, Stanley MC, Nwakaego OB. Comparative analysis of some haematological parameters in sickle cell patients in steady and crisis state at michael okpara University of agriculture, Umudike, Abia state, Nigeria. Int. J. Curr. Microbiol. App. Sci. 2014;3(3):1046-1050.
92. Ifeanyi EO, Uzoma GO. Malaria and The Sickle Cell Trait: Conferring Selective Protective Advantage to Malaria. J Clin Med Res. 2020; 2:1-4.

Citation: Obeagu EI. Chromium VI: A Silent Aggressor in Sickle Cell Anemia Pathophysiology. *Elite Journal of Haematology, 2024; 2(3):* 81-95