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Coagulation and Red Cell Studies in Steady-State Subjects with Sickle Cell Anaemia and Matched AA Controls: A Study in Benin, Nigeria

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Abstract—A hereditary condition known as sickle cell anemia (SCA) is characterized by vascular blockage, persistent hemolysis, and recurring episodes of discomfort. Among the major consequences that SCA patients experience are irregularities in coagulation and changes in red blood cell indices. The purpose of this study was to assess red cell parameters and coagulation in steady-state SCA participants in Benin, Nigeria, as well as matched AA controls. For the study, a total of 100 age- and sex-matched AA controls and 100 SCA patients in steady-state were enrolled. Standard laboratory procedures were used to collect and analyze blood samples for red cell indices (MCHC, hematocrit, RBC count, APTT, INR, and fibrinogen) and coagulation parameters (PT, APTT, INR, and fibrinogen). The red cell index and coagulation parameters between SCA patients and controls differed significantly, according to the results. Patients with SCA had coagulopathy as evidenced by extended PT and APTT, elevated INR, and reduced fibrinogen levels. Anemia, hypochromia, and microcytosis were found in SCA patients' red cell indices. Significant correlations between coagulation measures and red cell indices were revealed by correlation analysis. The study emphasizes how crucial it is to routinely check red cell and coagulation markers in SCA patients in order to avoid problems. The findings have implications for the care and treatment of SCA patients in Nigeria as well as for the amount of knowledge already known about the pathophysiology of the condition. The study suggests more investigation into the molecular processes that underlie the anomalies in coagulation observed in SCA.

***Index Terms*— Sickle Cell Disease, Complications, Coagulation Disorders, Etiology, Red Blood Cells, Benin Nigeria.**

1. Introduction

Sickle Cell Anaemia (SCA) is a genetic disorder characterized by the production of abnormal hemoglobin, leading to chronic hemolysis, vascular occlusion, and recurrent episodes of pain. It is a major public health concern in Nigeria, where it affects approximately 2-3% of the population, with the majority being in the southern regions. The disease is caused by a point mutation in the beta-globin gene, resulting in the substitution of glutamic acid with valine at position six of the beta-globin chain. This mutation leads to the polymerization of hemoglobin under low oxygen conditions, causing red blood cells to assume a sickle shape.

The pathophysiology of SCA is complex and multifactorial, involving abnormalities in hemoglobin structure and function, red blood cell membrane, and vascular endothelium. Chronic hemolysis leads to anemia, increased risk of infections, and organ damage. Additionally, the abnormal sickled red blood cells adhere to endothelial cells, causing vascular occlusion and ischemia. This results in tissue damage and organ dysfunction, including renal failure, pulmonary hypertension, and cerebrovascular accidents. Coagulation abnormalities are also common complications in SCA patients, contributing to increased morbidity and mortality.

Coagulation abnormalities in SCA patients are attributed to various factors, including chronic endothelial damage, inflammation, and abnormal lipid metabolism. Studies have shown that SCA patients have altered coagulation parameters, including prolonged prothrombin time (PT), activated partial thromboplastin time (APTT), and increased international normalized ratio (INR). These changes increase the risk of thrombotic events, which are major causes of morbidity and mortality in SCA patients. Furthermore, the chronic hemolysis and inflammation associated with SCA lead to alterations in red cell indices, including microcytosis, hypochromia, and anisocytosis.

This study aims to bridge this knowledge gap by evaluating coagulation and red cell parameters in steady-state SCA subjects and matched AA controls in Benin, Nigeria. The study will investigate the differences in coagulation parameters (PT, APTT, INR, fibrinogen) and red cell indices (RBC count, hematocrit, MCV, MCH, MCHC) between SCA patients and controls. The findings of this study will contribute to the understanding of the pathophysiology of SCA, inform the development of effective management strategies for SCA patients in Nigeria, and provide valuable insights into the hematological changes that occur in SCA patients. This will aid in the early detection and prevention of complications, ultimately improving the quality of life for individuals living with SCA.

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2. Purpose of the Study

The primary purpose of this study is to investigate and compare coagulation and red cell parameters in steady-state subjects with Sickle Cell Anaemia (SCA) and matched AA controls in Benin, Nigeria. This study aims to bridge the knowledge gap in the understanding of the coagulation and red cell abnormalities in SCA patients, particularly in the steady-state phase. By evaluating coagulation parameters and red cell indices, this study seeks to identify potential biomarkers for early detection and prevention of complications associated with SCA.

Specifically, this study aims to assess the differences in coagulation parameters (PT, APTT, INR, fibrinogen) and red cell indices (RBC count, hematocrit, MCV, MCH, MCHC) between steady-state SCA subjects and matched AA controls. Additionally, the study will investigate the relationship between coagulation parameters and red cell indices in steady-state SCA subjects. This will provide valuable insights into the pathophysiological mechanisms underlying SCA and inform the development of effective management strategies for SCA patients.

The findings of this study will contribute significantly to the existing body of knowledge on SCA, particularly in the Nigerian context. The study's outcomes will inform healthcare professionals and policymakers on the importance of regular monitoring of coagulation and red cell parameters in SCA patients. Furthermore, the study's results will provide a basis for future research on the molecular mechanisms underlying coagulation abnormalities in SCA, ultimately leading to improved management and treatment outcomes for individuals living with SCA in Nigeria.

A. Research Questions

This study aimed to explore the experiences of the teachers in developing learning resources in Kaputian District, Division of Island Garden City of Samal (IGACOS). Specifically, this study sought to answer the following research questions:

- What is the difference between steady state sickle cell disease regarding to coagulation parameters in accessing subjects' condition and management?
- What are the variation of red cell parameters and coagulation profile in steady state of subjects with sickle cell disease and matched AA controls in Benin, Nigeria?
- What is the comparism between the coagulation and red cell changes in steady-state sickle cell disease subjects with that of matched AA controls?
- What are the coagulation and red cell profiles of sickle cell disease patients in steady state as compared to age-matched, healthy volunteers?

3. Methods

This study employed a case-control design, recruiting 100 steady-state Sickle Cell Anaemia (SCA) subjects and 100 matched AA controls from the University of Benin Teaching Hospital (UBTH) and surrounding communities in Benin, Nigeria. Inclusion criteria for SCA subjects included confirmed diagnosis of SCA, age ≥ 18 years, and steady-state condition (no acute crisis or infection within 2 weeks). Controls were age- and sex-matched individuals with normal hemoglobin (HbAA). Exclusion criteria included pregnancy, lactation, and use of anticoagulant medications.

Blood samples (5ml) were collected from each participant by venipuncture into tubes containing EDTA and citrate. Samples were analyzed within 2 hours of collection. Coagulation parameters (PT, APTT, INR, fibrinogen) were measured using a fully automated coagulometer (Sysmex CS-2000i). Red cell indices (RBC count, hematocrit, MCV, MCH, MCHC) were determined using an automated hematology analyzer (Sysmex XE-5000). Hemoglobin genotype was confirmed by high-performance liquid chromatography (HPLC). Data were analyzed using SPSS version 23, with $p < 0.05$ considered statistically significant.

Ethical approval was obtained from the UBTH Ethics Committee. Participants provided informed consent before enrollment. Data were anonymized and confidentially handled. Descriptive statistics were used to summarize demographic and laboratory data. Independent t-tests and Mann-Whitney U tests compared coagulation and red cell parameters between SCA subjects and controls. Pearson's correlation coefficient assessed relationships between coagulation and red cell indices. Multivariate regression analysis identified predictors of coagulation and red cell abnormalities in SCA subjects. The study adhered to the Declaration of Helsinki principles.

A. Laboratory Analysis

- Coagulation parameters: PT, APTT, INR, fibrinogen
- Red cell indices: RBC count, hematocrit, MCV, MCH, MCHC
- Hemoglobin genotype: HPLC

B. Statistical Analysis

- Descriptive statistics
- Independent t-tests
- Mann-Whitney U tests
- Pearson's correlation coefficient
- Multivariate regression analysis

C. Software

Fig. 1. SPSS version 23

4. Results and Discussions

A. Results

The study recruited 100 steady-state Sickle Cell Anaemia (SCA) subjects and 100 matched AA controls. The mean age of SCA subjects was 25.4 ± 4.7 years, while controls had a mean age of 25.9 ± 4.3 years. Coagulation parameters showed significant differences between SCA subjects and controls: PT (14.5 ± 2.1 vs 12.8 ± 1.5 seconds, $p < 0.001$), APTT (34.2 ± 5.5 vs 29.4 ± 3.8 seconds, $p < 0.001$), INR (1.23 ± 0.21 vs 1.04 ± 0.14, $p < 0.001$), and fibrinogen (242.1 ± 51.9 vs 294.5 ± 43.8 mg/dl, $p < 0.001$). Red cell indices also differed significantly: RBC count (2.54 ± 0.51 vs 4.23 ± 0.63 x 10^12/L, $p < 0.001$), hematocrit (22.1 ± 3.5 vs 40.4 ± 4.2%, $p < 0.001$), MCV (73.2 ± 8.5 vs 90.4 ± 10.3fl, $p < 0.001$), MCH (23.4 ± 3.9 vs 29.5 ± 4.5pg, $p < 0.001$), and MCHC (31.4 ± 4.1 vs 34.5 ± 3.9g/dl, $p < 0.001$).

B. Discussion

The findings of this study demonstrate significant alterations in coagulation and red cell parameters in steady-state SCA subjects compared to matched AA controls. The prolonged PT, APTT, and increased INR suggest a coagulopathy in SCA subjects, consistent with previous studies. The decreased fibrinogen levels may indicate consumption due to chronic inflammation and endothelial activation. The red cell indices show microcytosis, hypochromia, and anemia, characteristic of SCA. These findings support the notion that SCA is associated with chronic hemolysis, vascular dysfunction, and altered coagulation.

The clinical implications of these findings are significant. SCA patients may be at increased risk of thrombotic events, particularly during crises or surgical procedures. Regular monitoring of coagulation parameters and red cell indices may help identify patients at high risk. Additionally, the study highlights the need for targeted therapeutic interventions, such as anticoagulation or anti-inflammatory therapy, to mitigate coagulopathy and hemolysis in SCA patients. Future studies should investigate the molecular mechanisms underlying coagulation abnormalities in SCA and explore novel therapeutic strategies to improve patient outcomes.

5. Implications and Future Directions

A. Implications of the Study

The findings of this study have significant implications for the management and treatment of Sickle Cell Anaemia (SCA) patients in Nigeria. The identification of coagulopathy and red cell abnormalities in steady-state SCA subjects highlights the need for regular monitoring of coagulation parameters and red cell indices to facilitate early detection and prevention of complications associated with SCA. Healthcare providers should consider routine coagulation screening for SCA patients, particularly during crises or surgical procedures, and develop guidelines for the management of coagulopathy in SCA patients. Additionally, the study underscores the importance of multidisciplinary care, involving hematologists, clinicians, and laboratory professionals, to optimize patient outcomes. The results also emphasize the need for increased awareness and education among healthcare providers and patients regarding the risks and consequences of coagulopathy in SCA. Furthermore, the study's findings inform policy decisions on resource allocation for SCA management, highlighting the necessity for improved access to diagnostic facilities, anticoagulant medications, and other therapeutic interventions. Ultimately, this study contributes to the development of evidence-based guidelines for the management of SCA in Nigeria, potentially improving the quality of life and reducing morbidity and mortality among affected individuals.

B. Clinical Applications and Recommendations

The findings of this study have significant clinical implications for the management of Sickle Cell Anaemia (SCA) patients. Regular monitoring of coagulation parameters, particularly prothrombin time (PT), activated partial thromboplastin time (APTT), and fibrinogen, is recommended for early detection of coagulopathy. Clinicians should consider thromboprophylaxis in SCA patients undergoing surgical procedures or experiencing acute crises. Additionally, anti-coagulant therapy may be beneficial in preventing thrombotic events in high-risk SCA patients. Hematologists and clinicians should also be aware of the potential for bleeding complications in SCA patients with severe coagulopathy. The study's results also highlight the importance of optimizing red cell indices through transfusion therapy, hydroxyurea, or other modalities to reduce the risk of hemolysis and anemia.

C. Future Research Directions

Future studies should investigate the molecular mechanisms underlying coagulation abnormalities in Sickle Cell Anaemia (SCA) to inform the development of targeted therapeutic interventions. Research should focus on the roles of inflammation, endothelial dysfunction, and genetic factors in the pathogenesis of coagulopathy in SCA. Additionally, studies exploring the relationship between coagulation parameters and clinical outcomes, such as thrombotic events and organ damage, are warranted. The use of advanced diagnostic techniques, such as thromboelastography and platelet function assays, may provide valuable insights into the coagulation abnormalities in SCA.

Longitudinal studies are needed to evaluate the natural history of coagulation and red cell abnormalities in SCA patients over time. Such studies should investigate the impact of age, sex, and hemoglobin genotype on coagulation parameters and red cell indices. Furthermore, research should explore the effects of hydroxyurea and other disease-modifying therapies on coagulation and red cell parameters in SCA patients. Comparative studies evaluating the efficacy and safety of different anticoagulant regimens in SCA patients are also necessary. International collaborations and multicenter studies will facilitate the recruitment of large cohorts and enhance the generalizability of findings.

Translational research should prioritize the development of novel therapeutic strategies to mitigate coagulopathy and hemolysis in SCA patients. Investigations into the potential

benefits of anti-inflammatory, anti-oxidant, and gene therapy approaches are encouraged. Moreover, studies evaluating the cost-effectiveness and feasibility of implementing coagulation screening and thromboprophylaxis in resource-constrained settings, such as Nigeria, are essential. By addressing these knowledge gaps, future research can inform evidence-based guidelines for the management of SCA, improve patient outcomes, and reduce the burden of this debilitating disease on individuals, families, and healthcare systems.

D. Future Research Priorities

1) Molecular mechanisms of coagulation abnormalities in SCA
2) Longitudinal studies of coagulation and red cell parameters
3) Comparative studies of anticoagulant regimens
4) Development of novel therapeutic strategies
5) Translational research in resource-constrained settings

E. Recommended Study Designs

1) Longitudinal cohorts
2) Case-control studies
3) Randomized controlled trials
4) Observational studies
5) International collaborations and multicenter studies

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