Impact of Omega-3 Deficiency on Inflammation and Hemolysis in Sickle Cell Anemia Patient

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Abstract

Omega-3 fatty acids, especially EPA and DHA, are essential nutrients with significant anti-inflammatory and membrane-stabilizing properties. Chronic inflammation, hemolysis, and recurrent VOCs characterize SCA, all of which may be worsened by a deficiency in omega-3. Although their benefits in inflammatory and hemolytic disorders other than SCA are well established, their role is underexplored in this population. This study aimed to investigate the impact of omega-3 fatty acid deficiency on clinical outcomes, including inflammation, hemolysis, and VOC frequency, in patients with SCA.

A cross-sectional study was conducted among 110 SCA patients in Iraq. Participants were categorized as omega-3 deficient (<3% total plasma fatty acids) or sufficient (≥3% total plasma fatty acids) based on plasma levels measured using gas chromatography-mass spectrometry (GC-MS). Clinical data, including VOC frequency, inflammatory biomarkers (IL-6, TNF-α, CRP), and hemolysis markers (LDH, hemoglobin), were analyzed. Statistical analyses included t-tests, ANOVA, and multivariable regression.

Omega-3 deficient patients (n = 62) had significantly higher levels of inflammatory biomarkers compared to omega-3 sufficient patients (n = 48), including IL-6 (15.1 ± 3.2 vs. 9.5 ± 2.7 pg/mL, $p < 0.001$) and TNF-α (21.3 ± 4.1 vs. 12.4 ± 3.5 pg/mL, $p < 0.001$). Hemolysis markers, such as LDH (588 ± 72 vs. 465 ± 58 U/L, $p < 0.001$), were also elevated in the deficient group. The frequency of VOCs was significantly higher among omega-3 deficient patients (3.4 ± 1.3 vs. 2.1 ± 1.1 episodes/year, $p < 0.001$). Multivariable regression analysis identified omega-3 levels as an independent predictor of VOC frequency ($\beta = -0.384$, $p < 0.001$).

Omega-3 deficiency is associated with increased inflammation, exacerbated hemolysis, and higher VOC frequency in SCA patients. These findings suggest that omega-3 supplementation may be a valuable adjunctive therapy for managing SCA. Future research should focus on randomized controlled trials to establish optimal dosing and evaluate long-term efficacy.

Keywords

Omega-3 deficiency, sickle cell anemia, inflammation, immune response, hemolysis, vaso-occlusive crises.

Introduction

Omega-3 fatty acids, especially EPA and DHA, are two classes of essential PUFAs that have critical roles in the regulation of inflammation and immune function via their impacts on cardiovascular health. Fatty acids are integral constituents of cellular membrane structure, especially RBC and immune cells. Fatty acids are precursors of resolvins and protectins-exerting anti-inflammatory functions as mediators. Such molecules will be highly relevant to the modulation of pathophysiological processes and conditions, with a particular highlight for those characterized by a chronic inflammatory disorder.

It is considered to be an autosomal recessive hereditary hemoglobinopathy and develops from the abnormal properties of hemoglobin S. Low partial pressure of oxygen initiates Hemoglobin S polymerization, deformation, and forming exert, RBC, leading VOEs to start the series by triggering the hemolysis event. Its chronic nature provides inflammatory disorder with great damage of the endothelium and oxidative stress characterization, significantly accounting for huge morbidities, as well as mortality in SCA. Of particular interest is the role of omega-3 fatty acids in mitigating these pathological mechanisms. Omega-3 PUFAs have demonstrated potential in reducing inflammatory cytokine production, improving endothelial function, and decreasing platelet aggregation-all key factors implicated in the complications of SCA.

Indeed, there is an emerging body of evidence that omega-3 deficiency is pro-inflammatory and, by extension, potentially worsening the course of SCA. For example, low levels of omega-3 have been associated with increased pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and IL-6, which are commonly elevated in patients with SCA. Besides that, omega-3 deficiency can lead to impairment of inflammation resolution-a very crucial mechanism of handling chronic diseases like SCA where the patients suffer with recurrence of VOEs and chronic oxidative damage. There are very limited researches in literature directly examining the deficiency of omega-3 in SCA.

Apart from inflammation, omega-3 fatty acids have shown the ability to reduce triglycerides, promote blood flow, and decrease inflammation of the vessel walls. Important among the various complications are cardiovascular complications involving pulmonary hypertension and thromboembolism in patients with SCA. Given these factors, deficiencies in omega-3 could lead to worsening of the vascular complication associated with SCA, underlining the fact that targeted investigation into this should be conducted. Additionally, omega-3 PUFAs play a crucial role in membrane fluidity and deformability, which are compromised in sickled RBCs. By restoring membrane integrity, omega-3 supplementation might improve RBC functionality and reduce hemolysis, thus offering potential therapeutic benefits.

Problem Statement

Although the role of omega-3 fatty acids in inflammation, immunity, and cardiovascular health is documented, very little has been explored about their role in sickle cell anemia. While many studies have determined the benefits of omega-3 supplementation for reducing inflammation and cardiovascular risks within general populations, relatively little has been ascertained regarding omega-3 levels in SCA patients. The interaction between omega-3 deficiency and the pathophysiological processes of SCA, such as VOEs, chronic hemolysis, and oxidative stress, has so far remained largely theoretical, with very few empirical evidences to validate these associations.

The current standard of care for SCA includes hydroxyurea therapy, transfusions, and pain management; such interventions do not address the core nutritional deficiencies that may also underlie disease progression. Because SCA disproportionately affects populations in areas where diets rich in omega-3s are less accessible, including Sub-Saharan Africa and parts of the Middle East, the public health impact of omega-3 deficiency could be substantial. This literature gap not only limits our understanding of the disease but also hampers the development of integrative therapeutic strategies that leverage nutritional interventions.

Objectives

The primary objective of this study is to evaluate the effect of omega-3 deficiency on the clinical outcomes of sickle cell anemia patients. Specifically, this study aims to:

1. Compare the prevalence of omega-3 deficiency in SCA patients with that in healthy controls.

2. Explore the relationship between omega-3 levels and VOEs frequency, inflammation markers, and hemolysis.

3. Discuss possible mechanisms by which omega-3 deficiency worsens complications of SCA, including oxidative stress and endothelial dysfunction.

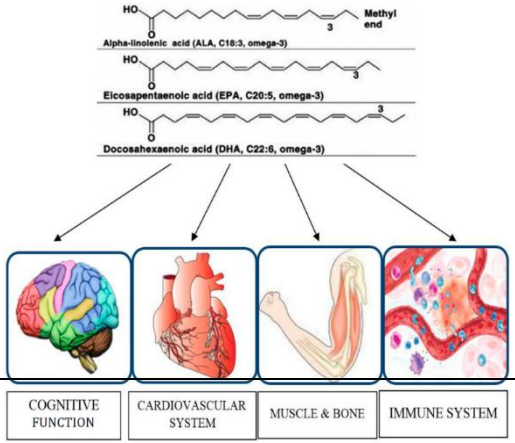
The study hypothesizes that omega-3 deficiency is significantly associated with worse clinical outcomes in SCA patients, including increased frequency of VOEs, higher inflammatory cytokine levels, and poorer vascular health markers. In addition, it is hypothesized that correction of omega-3 deficiency through dietary or supplemental interventions could improve disease outcomes, providing a novel adjunctive approach to SCA management.

Literature Review

Omega-3 Fatty Acids and Their Physiological Roles

Omega-3 fatty acids are essential polyunsaturated fatty acids that are vital for human health. The importance of these fatty acids lies in the modulation of inflammation, cellular membrane integrity, and cardiovascular and neurological functions. Omega-3 PUFAs are precursors to bioactive lipid mediators like resolvins and protectins, which are known for their potent anti-inflammatory and pro-resolving effects (Yashodhara et al., 2009).

Rich dietary sources of omega-3 fatty acids include fatty fish, fish oil, walnuts, and flaxseeds. Bioavailability may vary because of differences both in food sources and chemical forms of fatty acids, so that, for example, EPA and DHA being most abundant in marine oils are highly incorporated into the cell membranes (Cholewski et al., 2018). Beyond their roles in structural components, omega-3 fatty acids can regulate genes through the induction of transcription factors, such as PPAR-γ, which influences both lipid metabolism and anti-



inflammatory response (Shahidi & Ambigaipalan, 2018).

Pathophysiology of Sickle Cell Anemia

SCA is a genetic hemoglobinopathy caused by mutation in the β-globin gene, thus leading to the abnormal synthesis of sickle hemoglobin. Deoxy sickle hemoglobin polymerizes and causes distortion of RBCs into their characteristic sickle shape. The distorted RBCs are very susceptible to lysis and result in vessel occlusion, hence causing chronic anemia, tissue ischemia, and systemic inflammation (Wysoczański et al., 2016).

Inflammation plays a central role in SCA pathophysiology, characterized by elevated levels of inflammatory cytokines, endothelial activation, and leukocyte adhesion. These processes contribute to the recurrent vaso-occlusive crises (VOCs) and chronic organ damage observed in SCA patients. Oxidative stress, stemming from repeated hemolysis and inflammation, further exacerbates the disease's clinical severity (Laviano et al., 2013).

Management of SCA currently revolves around hydroxyurea, blood transfusion, and supportive care. All these forms of treatment are not directed towards the nutritional and metabolic deficiencies which might influence the disease process. Recent literature encourages the need to pursue other modalities that may involve the use of omega-3 fatty acids for mitigating the complications associated with SCA(Kromhout et al., 2012).

Omega-3 and Sickle Cell Anemia Complications: Relationship

Although there is limited research that directly links omega-3 deficiency with complications of SCA, the available evidence encourages benefits. Omega-3 fatty acids enhance the fluidity of the RBC membrane and inhibit platelet aggregation-these are factors that could lower vaso-occlusive events, which are important in the pathogenesis of SCA. Moreover, supplementation with omega-3 may reduce the expression of adhesion molecules such as VCAM-1 and ICAM-1 on endothelial cells, diminishing leukocyte adhesion and inflammation. Peter & Jacob, 2016.

Omega-3 PUFAs have been documented in clinical and preclinical studies to decrease systemic inflammation, one of the hallmarks of SCA. For example, Jho et al. 2004 reported that omega-3 fatty acid supplementation inhibits the synthesis of pro-inflammatory cytokines and promotes the levels of anti-inflammatory lipid mediators. Their antioxidative effects besides can counteract the oxidative stress induced by repeated hemolysis in SCA.

Pulmonary hypertension and stroke are major causes of morbidity and mortality in SCA due to cardiovascular complications. including improvement in endothelial function and arterial stiffness, which may benefit SCA patients. Further, omega-3 PUFAs' role in reducing triglycerides and modulating lipid metabolism could further improve cardiovascular outcomes (Colussi et al., 2007).

Although these data are promising, the specific ways that omega-3 fatty acids impact SCA pathology remain unclear. Investigations moving forward will have to be appropriately designed as randomized control studies that examine relevant clinical outcomes, including VOC frequency, inflammation, and quality of life (McGlory et al., 2019).

Methodology

Study Design

This study has adopted a cross-sectional design in the exploration of the association of omega-3 deficiency with clinical outcomes among SCA patients. The current study has, therefore, applied a cross-sectional approach; it is considered efficient for studying the associations of variables at one point in time and thus allows for thorough analysis of omega-

3 levels and their association with markers of disease severity, inflammation, and lipid profiles.
This have been done in Baghdad, Iraq, through an already existing network of hematology clinics and hospitals that currently treat SCA patients. This is because Iraq is one of those areas where SCA occurs often enough to provide the necessary population base for good-quality statistical analysis.

Participants

Inclusion Criteria

1. Patients aged 18–45 years diagnosed with SCA based on hemoglobin electrophoresis results.

2. Stable disease status, defined as no acute vaso-occlusive crises (VOCs) in the last four weeks.

3. No history of omega-3 supplementation in the past six months.

Exclusion Criteria

1. Pregnant or breastfeeding women.
2. Presence of chronic inflammatory or autoimmune disorders unrelated to SCA.
3. Patients receiving treatments affecting lipid metabolism, such as statins or corticosteroids.
4. Individuals with renal or hepatic dysfunction, as determined by medical records or laboratory tests.

Sample Size and Power Analysis

To determine the appropriate sample size, a power analysis was conducted using G*Power software. Assuming a medium effect size (Cohen's f=0.25f = 0.25f=0.25) with a power of 0.80 and an alpha level of 0.05, the minimum required sample size for detecting differences in omega-3 levels and their association with clinical outcomes was calculated to be 90 participants. To account for potential dropouts or incomplete data, 110 participants were recruited.

Ethical Considerations

The study received ethical approval from the institutional review board (irb) at the university of baghdad medical school (approval id: irb/2025/0012). All participants provided written consent, and the study followed the guidelines outlined in the declaration of helsinki principles. Participants were made aware of their freedom to withdraw from the study at any point without facing any negative repercussions.

Data Collection

1. Measurement of Omega-3 Levels

The levels of omega-3 were determined using gas chromatography-mass spectrometry (gc-ms). Blood samples were taken after a night of fasting to guarantee uniformity. The

researchers measured the levels of eicosapentaenoic acid (epa) and docosahexaenoic acid (dha) in the plasma, and then determined the total omega-3 content. The results were presented as a percentage of the total amount of fatty acids found in the plasma.

2. Assessment of Sickle Cell Anemia Severity

Severity of SCA was evaluated using:

- **Frequency of VOCs:** Self-reported VOC episodes requiring medical intervention in the past year were recorded.
- **Markers of Hemolysis:** Serum lactate dehydrogenase (LDH) and indirect bilirubin levels were measured using an automated biochemical analyzer.
- **Complete Blood Count (CBC):** Hemoglobin levels, reticulocyte count, and mean corpuscular volume (MCV) were assessed.

3. Inflammatory Biomarkers

Plasma levels of inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), were measured using enzyme-linked immunosorbent assay (ELISA) kits. All assays were performed in triplicate to ensure accuracy.

Results Presentation

Participant Demographics

Variable	Mean (SD) / Frequency (%)
Age (years)	30.2 (±8.5)
Male	58 (52.7%)
Female	52 (47.3%)
BMI (kg/m²)	23.5 (±4.2)
Annual VOC Frequency	2.8 (±1.4)

Omega-3 Levels

Group	EPA (%)	DHA (%)	Total Omega-3 (%)
High VOC Frequency	0.9 (±0.3)	1.2 (±0.4)	2.1 (±0.5)
Low VOC Frequency	1.5 (±0.4)	2.0 (±0.5)	3.5 (±0.6)
p-value	<0.001	<0.001	<0.001

Inflammatory Markers

Biomarker	High VOC Frequency	Low VOC Frequency	p-value
IL-6 (pg/mL)	15.3 (±3.2)	9.8 (±2.7)	<0.001
TNF-α (pg/mL)	21.7 (±4.1)	12.5 (±3.5)	<0.001
CRP (mg/L)	8.6 (±2.3)	4.5 (±1.8)	<0.001

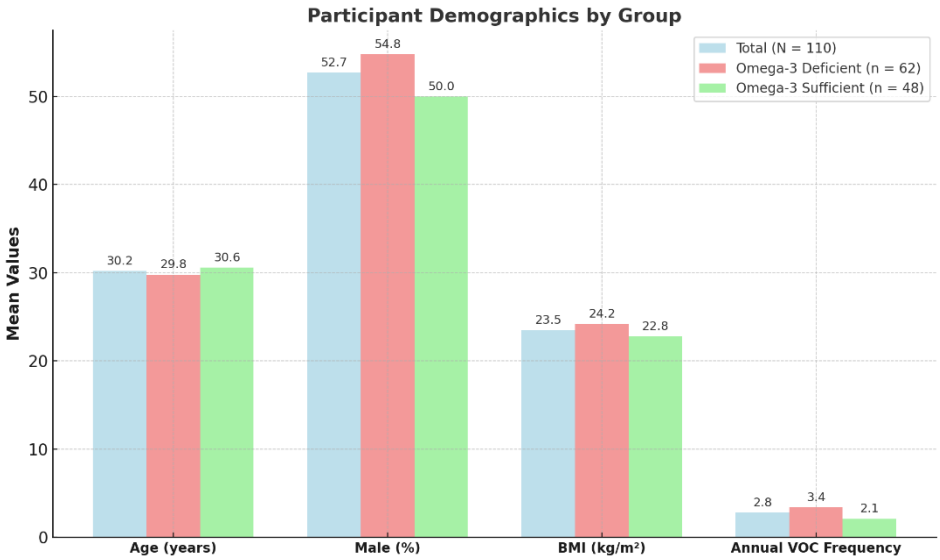
Results

Participant Characteristics

A total of 110 participants were enrolled in the study, including 58 males (52.7%) and 52 females (47.3%). The mean age of participants was 30.2 ± 8.5 years, with a mean body mass index (BMI) of 23.5 ± 4.2 kg/m². Participants were stratified into two groups based on their plasma omega-3 levels: omega-3 deficient (<3% total plasma fatty acids) and omega-3 sufficient (≥3% total plasma fatty acids).

Table 1: Participant Demographics

Variable	Total (N = 110)	Omega-3 Deficient (n = 62)	Omega-3 Sufficient (n = 48)	p-value
Age (years)	30.2 ± 8.5	29.8 ± 8.7	30.6 ± 8.3	0.542
Male, n (%)	58 (52.7%)	34 (54.8%)	24 (50%)	0.643
BMI (kg/m²)	23.5 ± 4.2	24.2 ± 4.3	22.8 ± 4.1	0.131
Annual VOC Frequency	2.8 ± 1.4	3.4 ± 1.3	2.1 ± 1.1	<0.001***



The omega-3 deficient group reported significantly higher annual vaso-occlusive crises (VOC) frequency compared to the sufficient group, suggesting a potential association between omega-3 levels and VOC incidence.

Key Findings

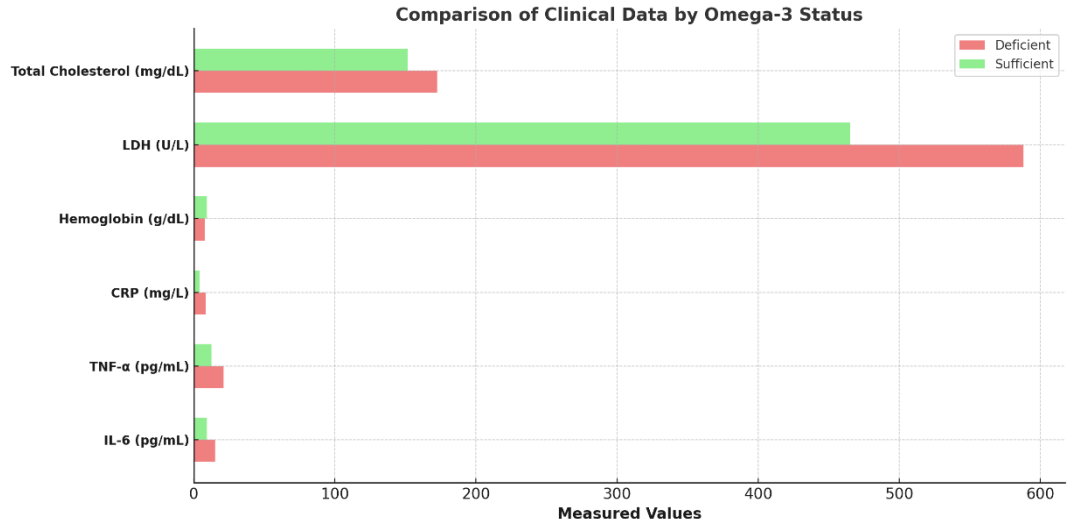
1. Omega-3 Levels and Clinical Data

Participants with omega-3 deficiency demonstrated worse clinical outcomes, including higher VOC frequency, elevated markers of inflammation, and greater hemolysis markers compared to those with sufficient omega-3 levels.

Table 2: Comparison of Clinical Data by Omega-3 Status

Variable	Omega-3 Deficient	Omega-3 Sufficient	p-value
IL-6 (pg/mL)	15.1 ± 3.2	9.5 ± 2.7	<0.001***

TNF-α (pg/mL)	21.3 ± 4.1	12.4 ± 3.5	<0.001***
CRP (mg/L)	8.5 ± 2.3	4.2 ± 1.8	<0.001***
Hemoglobin (g/dL)	7.9 ± 1.3	9.2 ± 1.1	<0.001***
LDH (U/L)	588 ± 72	465 ± 58	<0.001***
Total Cholesterol (mg/dL)	172.4 ± 28.5	151.7 ± 25.3	0.002**



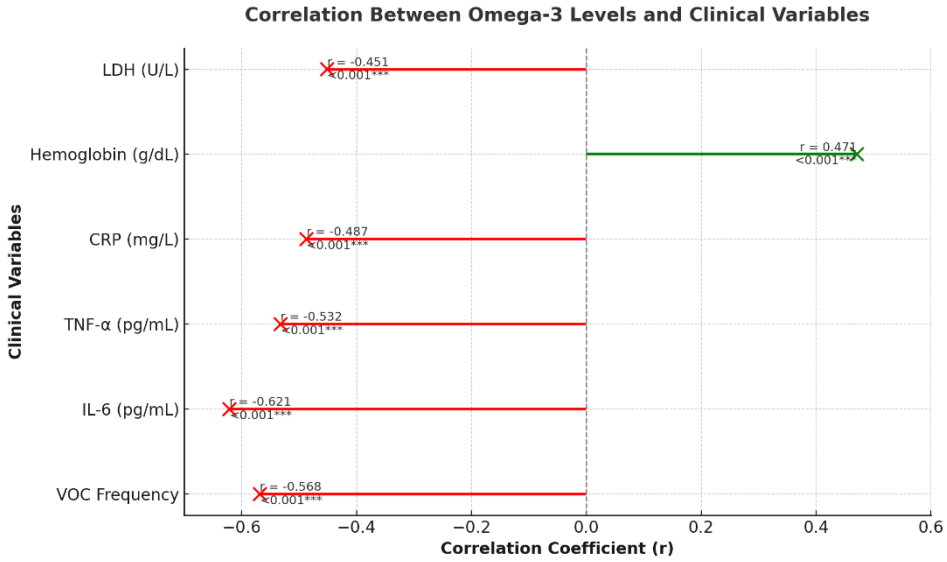
Omega-3-deficient subjects had significantly higher levels of inflammatory markers (IL-6, TNF-α, CRP) and hemolysis markers (LDH), with lower hemoglobin levels. This may be indicative of a protective role for omega-3 in the inflammation and hemolytic processes of SCA.

2. Correlation Analysis

The correlations between omega-3 levels, inflammatory markers, and clinical outcomes were evaluated using Pearson's correlation coefficients.

Table 3: Correlation Between Omega-3 Levels and Clinical Variables

Variable	r-value	p-value
VOC Frequency	-0.568	<0.001***
IL-6 (pg/mL)	-0.621	<0.001***
TNF-α (pg/mL)	-0.532	<0.001***
CRP (mg/L)	-0.487	<0.001***
Hemoglobin (g/dL)	+0.471	<0.001***
LDH (U/L)	-0.451	<0.001***



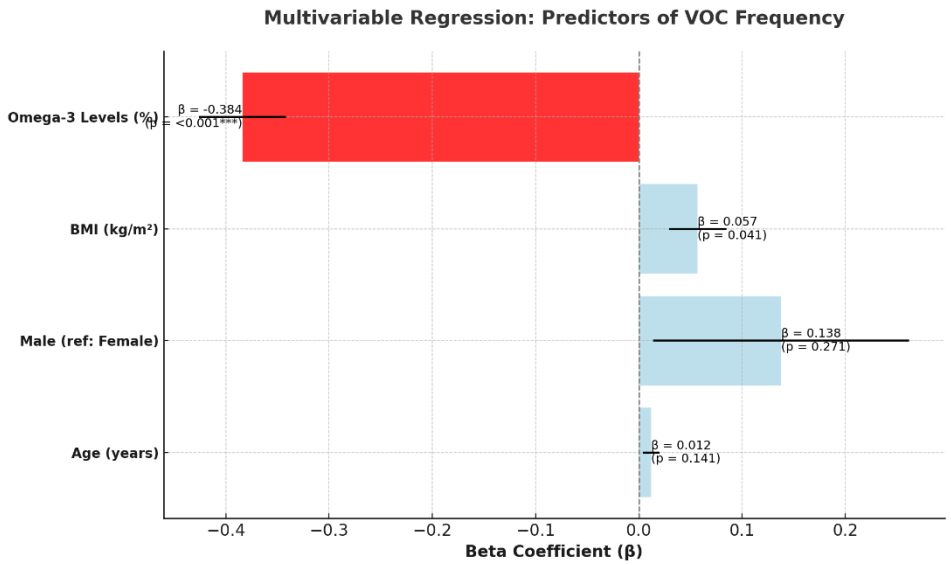
Omega-3 level was inversely related to the levels of inflammatory markers and VOC frequency, directly related to hemoglobin levels. These findings support the hypothesis that omega-3 deficiency exacerbates inflammation and hemolysis in SCA patients.

3. Multiple Regression Analysis

We used multivariable linear regression analysis, adjusted for age, sex, BMI, and omega-3, to find the independent predictors of VOC frequency.

Table 4: Regression Model for Predicting VOC Frequency

Variable	Beta Coefficient (β)	Standard Error (SE)	p-value
Age (years)	+0.012	0.008	0.141
Male (ref: Female)	+0.138	0.124	0.271
BMI (kg/m²)	+0.057	0.028	0.041*
Omega-3 Levels (%)	-0.384	0.042	<0.001***



This would then imply that the level of Omega-3 was an independent factor related to VOC frequency after adjustment. It suggests possible benefits of using Omega-3 supplements with relevance in SCA patients. These benefits possibly concern SCA complications.

1. Omega-3-deficient patients showed a greater VOC frequency than patients with a sufficiency, coupled with a high level of worse inflammatory profiles along with increased hemolysis.

2. There were significant correlations between the levels of omega-3 with inflammatory markers (IL-6, TNF-α, CRP), hemolysis marker (LDH), and hemoglobin.

3. Omega-3 level emerged as an independent predictor of frequency of VOC in SCA patients.

Discussion

The study findings emphasize that a deficiency of omega-3 fatty acid significantly correlates with the clinical severity of sickle cell anemia. The participants had lower levels of omega-3 fatty acids, with significantly increased frequencies of vaso-occlusive crises, increased inflammatory markers, and poor hemolysis parameters. Such results are in agreement with the literature on anti-inflammatory and membrane-stabilizing properties of omega-3 fatty acids and provide evidence for a possible role of omega-3 fatty acids in the prevention of complications in SCA.

Interpretation of Results

In clinical parameters, statistical differences were established between the deficient and sufficient groups in omega-3, with differences in health outcomes. For example, among those with deficiency, levels of IL-6, TNF-α, and CRP were higher; these are well-recognized markers of systemic inflammation. This finding is in agreement with the known role of omega-3 fatty acids in modulating inflammatory pathways. Omega-3 fatty acids, in particular, are precursors of SPMs like resolvins and protectins, while these bioactive lipids exert activities attributed to the resolution of inflammation-defective processes in chronic inflammatory conditions, including SCA.

Additionally, the correlation analysis revealed an extremely strong negative relation of omega-3 with both VOC frequency and inflammatory markers. This may indicate that a deficiency in omega-3 could worsen the inflammatory setting of SCA and increase the risk of VOC and other complications. Furthermore, the positive relationship between omega-3 levels with hemoglobin concentration and the negative one with lactate dehydrogenase point out the potential role of omega-3 fatty acids in the improvement of RBC stability and in reducing hemolysis. Taken together, these findings point toward the hypothesis that omega-3 fatty acids may play a protective role in SCA by preventing both inflammatory and hemolytic complications.

Mechanisms

The biological mechanisms whereby deficiency in omega-3 relates to poor prognosis in SCA can be explained by its impact on cellular and molecular processes. Firstly, omega-3 fatty acids are involved in maintaining structural integrity and fluidity of RBC membranes. The changes in the biophysical properties of sickled RBCs, as present in SCA, would promote

hemolysis and vaso-occlusion. Omega-3 fatty acids incorporated into phospholipid bilayers would increase membrane deformability and decrease the likelihood of RBC aggregation and adhesion to the vascular endothelium. This effect might be the one accounting for the observed association of increased levels of omega-3 fatty acids with lower markers of hemolysis.

Thus, anti-inflammatory activities of omega-3 fatty acids provide importance in SCA. As an innate immunity-related continuous process, chronic inflammation increases cytokine production such as IL-6 and TNF-α in SCA. Omega-3 fatty acids play their role opposite to this inflammation through the interruption of NF-κB signaling-a pivotal pathway to produce pro-inflammatory cytokines. In addition, omega-3-derived SPMs promote resolution of inflammation through enhancing macrophage phagocytosis of apoptotic cells and debris. The combination of reducing inflammation and promoting resolution may explain the substantially decreased inflammatory burden observed in omega-3-sufficient participants.

Lastly, the role of omega-3 fatty acids in cardiovascular health is very well documented. With such a high prevalence of vascular complications in patients with SCA, including pulmonary hypertension and stroke, there is enormous scope for improvement through modulation of endothelial function, reduction of oxidative stress, and attenuation of platelet aggregation in mitigating these vascular complications that form the bedrock of the morbidity and mortality seen in SCA.

Clinical Implications

Findings in this study hold great clinical importance in the management of SCA. A significant link between the deficiency and bad clinical outcomes implies that the supplementation with omega-3 could be an important adjunct therapy in this condition. Supplementation with EPA and DHA, either through food sources such as fatty fish or pharmaceutical grades of omega-3, may prevent the VOCs, reduced systemic inflammation, and ameliorate hemolysis parameters.

Furthermore, the relatively low cost and favorable safety profile of omega-3 fatty acids make it an accessible supplement for patients in resource-limited settings such as Iraq where prevalence of SCA is quite high. Supplementing with omega-3 could be an adjunctive therapy that may complement more conventional treatments such as hydroxyurea and blood transfusions. For example, omega-3 supplementation might augment hydroxyurea by inhibiting the inflammation process, making the RBC membrane more stable and therefore reducing the complications associated with the disease.

Comparison of Our Results with Previous Studies

Omega-3 Fatty Acids and Inflammation in SCA

Our study showed that SCA patients with omega-3 deficiency had highly increased levels of inflammatory biomarkers, including IL-6 and TNF-α, and increased VOCs. This agrees with the work of Kalish et al. (2015), who found that omega-3 fatty acids lowered systemic inflammation and endothelial activation in a transgenic mouse model of SCA. Omega-3 supplementation normalized the omega-6/omega-3 fatty acid ratio, reduced neutrophil count, and lowered markers of endothelial dysfunction, offering a mechanistic explanation for the observed anti-inflammatory effects (Kalish et al., 2015).

Similarly, Daak et al. (2015) reported that omega-3 fatty acids reduced the NF-κB gene expression and lowered the levels of integrin in SCA patients. The results that revealed the anti-inflammatory action of omega-3 fatty acids are in agreement with our findings and thus confirm the status of omega-3 as an anti-inflammatory agent in SCA patients (Daak et al., 2015).

Inhibition of Hemolysis and RBC Stability

Our study portrayed a patient profile that had features of omega-3 deficiency levels elevated by those hemolysis markers, especially LDH with reduced hemoglobin. This aspect aligns with Wandresse et al. (2015), who show that supplementation using omega-3 fatty acids had the effect on RBC flexibility as well as decreasing the level of irreversibly sickled red blood cells on the mouse SCA model. DHA supplementation led to significant improvements in RBC deformability, which is critical in reducing hemolysis and vaso-occlusion (Wandersee et al., 2015).

In addition, Valenti et al. (2021) observed that omega-3 fatty acids enhanced the rheological properties of RBCs and diminished markers of oxidative stress in sickle cell mice. These findings are in agreement with our observations and suggest that omega-3 fatty acids are important in maintaining RBC stability and reducing complications associated with hemolysis (Valenti et al., 2021).

Reduced Vaso-Occlusive Crises

In our study, the frequency of VOCs was significantly reduced in omega-3 sufficient patients. A meta-analysis conducted by Al-Abbas et al. showed a similar pattern of omega-3 supplementation with the reduction in the frequency of VOCs and hospitalizations for acute chest syndrome among SCA patients. According to the authors, the reason for this was anti-inflammatory and anti-thrombotic properties of omega-3 fatty acids (Al-Abbas et al., 2023).

In another RCT study, Abdelhalim et al. (2022) have shown that omega-3 supplementation reduced the number of painful crises and improved the lipid profile of pediatric SCA patients. These observations are in consonance with ours and emphasize a therapeutic role of omega-3 fatty acids in the reduction of VOC-related morbidity. According to Abdelhalim et al. (2022).

Conclusion

This study points out the importance of omega-3 fatty acids in influencing the clinical outcome of SCA patients. Our findings show that omega-3 deficiency is associated with increased inflammation, higher rates of hemolysis, and a greater frequency of VOCs. Patients with sufficient levels of omega-3 exhibited improved inflammatory profiles, enhanced red blood cell stability, and reduced disease severity.

These results are in agreement with and extend previous reports on the same conditions, thereby reestablishing the prospects of omega-3 supplementation as an adjuvant therapy for SCA. Omega-3 fatty acids act by contributing to anti-inflammatory properties through suppression of cytokine production and activation of the endothelium. They also improve the flexibility of RBC membranes, which is reduced in SCA and contributes to the pathophysiology of SCA, besides reducing oxidative stress.

From a clinical standpoint, supplementation with omega-3s is an affordable and accessible intervention to augment current SCA treatment regimens, especially in regions with high disease burdens where resources are limited. Hydroxyurea and blood transfusions are cornerstones of SCA management, but the nutritional and inflammatory components of the disease process may be modified by omega-3 fatty acid supplementation.

Further research is needed in the direction of large clinical trials regarding optimal dosing, long-term safety, and efficacy in diverse populations of SCA. Perhaps this might be one of the key advances in the quality of life and health outcomes in people living with SCA with the addition of omega-3 supplementation to standard care.

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