ORIGINAL ARTICLE

The Impact of Docosahexaenoic Acid (DHA) Supplementation on Calcium Levels in Third Trimester Pregnant Women with Chronic Energy Deficiency (CED): A Correlational Study

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ABSTRACT

Background: Chronic Energy Deficiency (CED) during pregnancy represents a critical health challenge, especially in developing regions, where it significantly threatens maternal and fetal well-being. Docosahexaenoic Acid (DHA), an essential omega-3 fatty acid, plays a pivotal role in fetal neurodevelopment and maternal health. However, the impact of DHA supplementation on maternal calcium levels, particularly among pregnant women affected by CED, has not been extensively studied. This study evaluate the correlation between DHA supplementation and calcium levels in third-trimester pregnant women with CED, with the goal of improving outcomes for this vulnerable population. Method and Results: This research uses experimental cohort study design with a quantitative approach, using non-probability sampling techniques such as quota and purposive sampling, and involving a total of 24 participants. Statistical analysis revealed a significant increase in calcium levels following DHA supplementation, with a p-value of 0.007 (<0.05), indicating a notable impact of the intervention. The mean calcium levels post-treatment were higher than pre-treatment, demonstrating the efficacy of DHA supplementation in improving calcium levels. Further analysis showed no significant correlation between pre-supplementation calcium levels and Body Mass Index (BMI) (p = 0.622, > 0.05). However, a significant correlation was found between post-supplementation calcium levels and BMI (p = 0.002, < 0.05). These findings indicate a positive correlation between DHA supplementation and calcium levels in pregnant women with CED during the third trimester. However, further investigation is needed to fully understand the relationship between calcium levels and BMI.

Conclusion: This study lays the groundwork for future research aimed at optimizing therapeutic interventions or supplementation strategies to improve the nutritional status of underweight pregnant women.

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Introduction

Chronic Energy Deficiency (CED) is a persistent and severe form of undernutrition that affects a substantial number of pregnant women. particularly in developing regions. Characterized by inadequate intake of calories and nutrients, CED poses significant risks to both maternal and fetal health, including increased susceptibility to infections, complications during childbirth, and adverse birth outcomes such as low birth weight and impaired fetal development. The condition underscores the critical need for effective nutritional interventions to support the health and well-being of both mother and child during pregnancy.^{1,2}

Pregnant women with CED are pregnant women with nutritional deficiencies such as calories and protein. So that it affects the health of the mother and her baby. Pregnant women can be known to experience CED by looking at UAC (upper arm circumference) and < 23.5 cm. The 4,656,382 pregnant women in Indonesia, 451,350 are at risk of chronic energy deficiency and according to the Ministry of Health in 2020 the incidence rate was 9.7% in 2020. Then the basic health survey in 2018, the prevalence of pregnant women at risk of chronic energy deficiency (CHD) in Indonesia is 17.3 percent.³

Docosahexaenoic Acid (DHA), an omega-3 fatty acid, is essential for fetal neurodevelopment and maternal health. DHA plays a vital role in the development of the fetal brain and retina, and it has been associated with positive pregnancy outcomes such as prolonged gestation and reduced risk of preterm birth. Despite its recognized benefits, the impact of DHA supplementation on other physiological aspects, such as calcium metabolism, particularly in pregnant women affected by CED, has not been extensively studied.⁴

Calcium is a crucial mineral required for the development of the fetal skeletal system and the maintenance of maternal bone health. Pregnancy significantly increases the demand for calcium, and deficiencies can lead to serious complications such as gestational hypertension and preeclampsia. In the context of CED, where nutritional deficits are prevalent, understanding how DHA supplementation might influence calcium levels is of particular importance.⁵

This study aims to explore the correlation between DHA supplementation and calcium levels in pregnant women with CED during their third trimester. This research provide insights into potential nutritional strategies and contributing to better health outcomes for mothers and their babies.

Methods

This research uses experimental cohort study design with a quantitative approach, using nonprobability sampling techniques such as quota and purposive sampling, and involving a total of 24 participants. The inclusion criteria in this study were pregnant women registered at Made and Simomulyo Health Center (gestational age 28-40 weeks or 3rd trimester) and pregnant women with CED (UAC < 23.5 cm). The exclusion criteria for this study were gestational age less than 28-40 weeks or less than the 3rd trimester and UAC > 23.5 cm, as well as samples that did not routinely take DHA supplements and withdrew from the study.

Results

In this study we conducted several analyses of respondents through the characteristics of

respondents age, gestational age, weight, height, body mass index (BMI), calcium pre and post examination.

Characteristics	Ν	Minimum	Maximum	Median	Mean	St Deviation
Respondents Age	24	22	39	28	29.37	4,79
Gestational Age	24	28	39	29,0	31,0	3,765
Weight	24	38,0	52,0	43.500	44.258	4,5154
Height	24	144	170	155.50	156.167	7.9052
BMI	24	17,21	18.61	18.3200	18.1079	0.43790
Calcium Pre	24	1.6	13.6	6.700	6.629	2.7765
Calcium post	24	1.2	17.7	8.700	8.842	4.2095

Table 1 Research Characteristics

In this research characteristic, the number of respondents was 24 underweight pregnant women. The age characteristics of respondents are in the reproductive age category, namely 22 years to 33 years, then the gestational age represents the three trimesters of pregnancy, from 6 weeks to 27 weeks of gestation, so this study can represent each trimester of pregnancy. The characteristics of height and weight are limited to the underweight category.

Table 2 Normality of Research Data

Characteristics	Ν	Minimum
Respondents Age	24	.163
Gestational Age	24	<0,0001
Weight	24	.157
Height	24	.336
BMI	24	.001
Calcium Pre	24	.772
Calcium post	24	.888

In the normality test of the research data, it was found that BMI, gestational age, body weight data were abnormal because p < 0.05, while pre and post Calcium and Delta data were normal because p > 0.05.

Based on the results of the pre and post Calcium data normality test, it was declared normal because the p value> 0.05, so the comparison test used the Paired T test.

Table 3 Comparative Analysis of Calcium Pre

and Post Treatment

	Mean <u>+</u> SD	Р
Calcium	6,62 <u>+</u> 2,77	0,007
Pre		
Calcium	8,8 <u>+</u> 4,20	
Post		

Based on the results of the normality test, the pre Calcium data is normal while BMI is abnormal, so the test of the relationship uses the Spearman test.

 Table 4 Analysis of the Relationship Between

Pre-Treatment Calcium Levels and BMI

	Mean <u>+</u> SD	Р
Calcium	6,62 <u>+</u> 2,77	0,723
Pre		
BMI	18.10 ± 0.437	

Based on the results of the normality test, the post Calcium data is normal while BMI is abnormal, so the test of the relationship between post Calcium and BMI uses the Spearman test.

	Mean <u>+</u> SD	Р
Calcium	8,8 <u>+</u> 4,20	0,002
Post		R = 0,608
BMI	18,10 <u>+</u> 0,437	-

 Table 5 Analysis of the Relationship Between

 Pre-Treatment Calcium Levels and BMI

Discussion

DHA increase plasma calcium levels, and thus increase bone mass; hence, our data confirm the valuable effects of PUFAs as the source of DHA on bone formation. Heaney et al. found that ω -3 DHA supplementation increased calcium absorption in humans. DHA maintain Ca and P homeostasis and do not cause disturbances in their nutritional balance. Numerous studies have indicated that DHA and their metabolites play important roles in regulating bone metabolism. The connection between DHA and bone metabolism might be attributed to various suggested mechanisms, including the regulation of osteoclast and osteoblast activity and differentiation, along with alterations in the fatty acid composition of bone cell membranes. DHA have been shown to reduce osteoclast activity while enhancing osteoblast Additionally, function. dietary supplementation with long-chain PUFAs has exhibited a protective effect against bone loss associated with aging.⁶ Malondialdehyde, a byproduct of lipid peroxidation, is closely linked with oxidative stress.⁷ In our study, DHA treatment significantly reduced oxidative stress across all groups. DHA supplementation notably decreased MDA levels in both serum and liver, as well as reduced hepatic oxidative stress. The reported immunological effects of DHA, including its role in improving pro-inflammatory status and combating oxidative stress, suggest it may help prevent or treat lipid peroxidation.⁸ One possible mechanism is that osteocytes influence the development and function of osteoblasts and osteoclasts. Apoptotic osteocytes release proinflammatory cytokines like TNF- α , which promote osteoclastogenesis. Treatment with DHA lowered inflammation, and recent research shows that DHA intake effectively reduces inflammatory markers by lowering TNF- α level.⁹

The findings from this study underscore the potential benefits of Docosahexaenoic Acid (DHA) supplementation in improving calcium levels among third-trimester pregnant women with Chronic Energy Deficiency (CED). The results of the Paired T-test comparing calcium levels before and after treatment revealed a p-value of 0.007, which is below the significance threshold of 0.05, indicating a statistically significant difference. The mean calcium levels post-treatment were notably higher than pre-treatment levels, confirming that the administered treatment had a positive impact, leading to an increase in calcium levels. Our findings are consistent with the research conducted by Nami Kim et al., which demonstrated that DHA supplementation enhances the intensity of green fluorescence, a marker of calcium concentration in their study, reflecting an increase in intracellular Ca²⁺ levels.¹⁰ This alignment supports the conclusion that DHA administration contributes to elevated calcium levels. Given the lack of previous research specifically addressing the impact of DHA on calcium levels in underweight pregnant women during the third trimester, our results provide a valuable foundation for future studies.¹¹ The significant increase in calcium levels postsupplementation suggests that DHA may influence calcium metabolism, potentially through

mechanisms related to its anti-inflammatory properties and its role in enhancing nutrient absorption.¹² This is particularly relevant in populations with CED, where nutritional deficiencies are prevalent and can have detrimental effects on both maternal and fetal health.¹³

The normality test results showed that pretreatment calcium levels were normally distributed, while BMI data were not. The analysis resulted in a p-value of 0.622, exceeding the significance threshold of 0.05, suggesting no statistically significant correlation between pretreatment calcium levels and BMI. However, the analysis of the relationship between post-treatment calcium levels and BMI revealed a statistically significant association. The Spearman correlation coefficient (r) was 0.608, a positive value, indicating that higher post-treatment calcium levels are correlated with higher BMI. The coefficient of 0.608 reflects a strong relationship, accounting for 60.8% of the variance. These findings are consistent with the study by Xiao-hua Ren et al., which demonstrated a significant association between total serum calcium levels and the prevalence of overweight and obesity.¹⁴ In their research, individuals in the highest quartile of serum calcium levels were found to have a higher risk of being overweight or obese compared to those in the lowest quartile. This suggests that elevated serum calcium may be a marker or contributing factor to increased body weight, supporting the correlation observed in our study.¹⁵ In contrast, the study by Abdelmarouf H. Mohieldein et al. found a negative correlation between serum calcium concentrations and BMI (r = -0.393, p = 0.003), suggesting an inverse relationship that contradicts our findings. This discrepancy highlights the complexity of the calcium-BMI relationship and underscores the need for more targeted research to explore the underlying mechanisms. Notably, no previous studies have specifically examined the relationship between post-treatment calcium levels and BMI in underweight pregnant women during the third trimester. Thus, our findings not only fill a critical gap in the current literature but also lay the groundwork for future research to better understand the physiological and clinical implications calcium metabolism of during pregnancy.16

Conclusion

This study demonstrates that Docosahexaenoic Acid (DHA) supplementation in third-trimester pregnant women with Chronic Energy Deficiency (CED) has a significant positive impact on calcium levels. The findings indicate a strong, positive correlation between increased calcium levels following DHA supplementation and Body Mass Index (BMI). However, the study also highlights the need for further research to explore the underlying mechanisms of this relationship and to of DHA assess the long-term effects supplementation on both maternal and fetal outcomes.

Conflict of Interest

No conflict of interest in this study

References

 Fitria SY, Suhartini, Yani RWE. Analysis of Determinant Factors of Chronic Energy Deficiency (CED) in Pregnant Women With Modification of Lawrence Green and Snehandu B. Kar's Theories. J Ilmu Kesehat Masy. 2024;14(3):381-92.

- Angraini DI, Aryani LD, Sari MI, Imantika E. The Effect of Chronic Energy Deficiency and Protein Intake on the Incidence of Preeclampsia in Dr . H . Abdul Moeloek Hospital Lampung Province. Int Conf Innov Soc Sci Educ [Internet]. 2020;705–15. Available from: http://repository.lppm.unila.ac.id/25219/
- Siahaan SC, Henderi H, Sudibjo, Safitiri NPD, Wakas BE, Pratama MFI. Intervensi Ibu Hamil Dengan Kurang Energi Kalori Melalui Suplementasi Mikronutrien Di SurabayaTahun 2019. Maj Kedokt Andalas [Internet]. 2021;44(1):17–27. Available from: http://jurnalmka.fk.unand.ac.id
- Basak S, Mallick R, Banerjee A, Pathak S, Duttaroy AK. Maternal supply of both arachidonic and docosahexaenoic acids is required for optimal neurodevelopment. Nutrients. 2021;13(6):1–28.
- Ryan BA, Kovacs CS. Maternal and fetal vitamin D and their roles in mineral homeostasis and fetal bone development. J Endocrinol Invest [Internet]. 2021;44(4):643–59. Available from: https://doi.org/10.1007/s40618-020-01387-2
- 6. Rozner, R., Vernikov, J., Griess-Fishheimer, S., Travinsky, T., Penn, S., Schwartz, B., Mesilati-Stahy, R., Argov-Argaman, N., Shahar, R., & Monsonego-Ornan, E. (2020). The Role of Omega-3 Polyunsaturated Fatty Acids from Different Sources in Bone Development. *Nutrients*, *12*(11), 3494. https://doi.org/10.3390/nu12113494
- Rozner, R., Vernikov, J., Griess-Fishheimer, S., Travinsky, T., Penn, S., Schwartz, B., Mesilati-

Stahy, R., Argov-Argaman, N., Shahar, R., & Monsonego-Ornan, E. (2020). The Role of Omega-3 Polyunsaturated Fatty Acids from Different Sources in Bone Development. *Nutrients*, *12*(11), 3494. https://doi.org/10.3390/nu12113494.

- 8. Díaz, M., Mesa-Herrera, F., & Marín, R. (2021).
 DHA and Its Elaborated Modulation of Antioxidant Defenses of the Brain: Implications in Aging and AD Neurodegeneration. *Antioxidants (Basel, Switzerland)*, 10(6), 907. https://doi.org/10.3390/antiox10060907
- Elbahnasawy AS, Valeeva ER, El-Sayed EM, Stepanova NV. Protective effect of dietary oils containing omega-3 fatty acids against glucocorticoid-induced osteoporosis. J Nutr Heal. 2019;52(4):323–31.
- Cordiano R, Di Gioacchino M, Mangifesta R, Panzera C, Gangemi S, Minciullo PL. Malondialdehyde as a Potential Oxidative Stress Marker for Allergy-Oriented Diseases: An Update. *Molecules*. 2023; 28(16):5979. https://doi.org/10.3390/molecules28165979
- 11. Kim N, Lee JO, Lee HJ, Kim HI, Kim JK, Lee YW, et al. Endogenous ligand for GPR120, docosahexaenoic acid, exerts benign metabolic effects on the skeletal muscles via AMPactivated protein kinase pathway. J Biol Chem [Internet]. 2015;290(33):20438–47. Available from:

http://dx.doi.org/10.1074/jbc.M115.657379

 Karageorgou D, Rova U, Christakopoulos P, Katapodis P, Matsakas L, Patel A. Benefits of supplementation with microbial omega-3 fatty acids on human health and the current market scenario for fish-free omega-3 fatty acid. Trends Food Sci Technol [Internet]. 2023;136:169–80. Available from: https://www.sciencedirect.com/science/arti cle/pii/S0924224423001346

- 13. Chen, J. M., Wu, T. Y., Wu, Y. F., & Kuo, K. L. (2023). Association of the serum calcium level with metabolic syndrome and its components among adults in Taiwan. Archives of endocrinology and metabolism, 67(5), e000632. https://doi.org/10.20945/2359-3997000000632
- 14. Stavrinou PS, Andreou E, Aphamis G, Pantzaris M, Ioannou M, Patrikios IS, et al. The effects of a 6-month high dose omega-3 and

omega-6 polyunsaturated fatty acids and antioxidant vitamins supplementation on cognitive function and functional capacity in older adults with mild cognitive impairment. Nutrients. 2020;12(2):1–17.

- 15. Ren XH, Yao YS, He LP, Jin YL, Chang WW, Li J, et al. Overweight and obesity associated with increased total serum calcium level: Comparison of cross-sectional data in the health screening for teaching faculty. Biol Trace Elem Res. 2013;156(1–3):74–8.
- 16. Mohieldein AH, Moshawah SAA, Elhabiby MI, Mustafa AA. Association of Total Serum Calcium Level with Obesity Markers (Body Mass Index and Waist Circumference) among Healthy Young Saudis. Pakistan J Med Heal Sci. 2023;17(4):348–51.