

EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Title: Effect of omega-3: Docosahexaenoic acid (DHA) supplementations on the neonatal birth weight among anemic pregnant women

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EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Abstract

The need for omega-3 fatty acids, especially docosahexaenoic acid (DHA), during pregnancy has received much attention, but evidence of its effects on birth outcomes for anemic pregnant women is still limited. **Aim:** examine the effect of omega-3(DHA) supplementations on the neonatal birth weight among anemic pregnant women. **Design:** quasi-experimental non-equivalent control group design. **Sample:** Purposive sample of a total of 240 anemic women divided into two groups according to certain inclusion criteria. **Setting:** antenatal care outpatient clinic and delivery unit (section10- emergency) at El Manial Maternity Hospital. **Tools: five tools were used** for data collection in this study. **Results:** There were highly statistically significant differences between both groups regarding neonatal gestational age, and anthropometric measurements. 61.7% of mothers in the study group as compared to 45.8% in the control group delivered neonates at ± 39 wks of gestation, at p-value = 0.0001. and mean neonatal weight 2608.3 ± 459.1 in the study group as compared to 2375 ± 219.4 in the control group P= 0.0001. **Conclusion:** supplementation with omega3 (DHA) is effective in improvement gestational age and anthropometric measurements (weight of the neonate, length, head circumference and chest circumference). Therefore, this study **recommended** raise awareness of anemic pregnant women who had previous low birth weight in antenatal clinic regarding the importance of higher n-3 FAs intake during pregnancy to reduce the occurrence of low birth weight and Further RCTs & systematic review researches exploring the effect of n-3 FAs intake during pregnancy on the occurrence of low birth weight.

Keywords: omega-3 fatty acids, docosahexaenoic acid (DHA), and anemic pregnant women.



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Introduction

Maternal nutritional status is well known to be an important determinant of placental and fetal growth,¹ historically, recommendations for maternal nutrition have emphasized protein, energy, vitamin, and mineral requirements, but dietary lipids, especially essential fatty acids (EFAs), have received attention recently². Among the different nutrients, long chain poly unsaturated fatty acids (LCPUFA) like docosahexaenoic acid (DHA) and arachidonic acid (ARA) are vital during pregnancy for the fetus since they form structural constituents of the membrane lipids of the developing brain and central nervous system .³

DHA is a key nutrient for the metabolism, especially during pregnancy. The benefits of DHA are based on its anti-inflammatory and anti-oxidative properties' improving both placental blood flow and amniotic membranes resistance and it is well established during the last trimester of pregnancy⁵. Fetal growth requires the presence of normal placental function and an adequate maternal nutritional status, so several studies reported the effect of DHA supplementation on newborn weight ⁷

Anemia during pregnancy contributes to 20% of all maternal deaths. In developing countries, the cause of anemia during pregnancy is multifactorial and includes nutritional deficiencies of iron, folate, and vitamin B12 and also parasitic diseases⁸. Anemia in pregnancy is one of the factors associated with adverse maternal and fetal outcome like antepartum hemorrhage, postpartum hemorrhage, maternal deaths and increased incidence of premature births, low birth weight babies and high perinatal mortality⁹.



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Significance of the study

The need for omega-3 fatty acids, especially docosahexaenoic acid (DHA), during pregnancy has received much attention, but evidence of effects on birth outcomes for anemic pregnant women is still limited.

Meanwhile, there are a scanty of researches which integrate DHA supplements with anemic pregnant women and neonatal birth weight, such as Muthayya, (2009) who conducted study in India only on maternal nutrition and low birth weight found out nearly half of the pregnant women still suffer from varying degree of anemia, with the highest prevalence in India. Of specific concern is compliance with iron supplementation, cultural beliefs regarding diet in pregnancy, and the issue of nutrition supplementations and fortification. The coexistence of risk of LBW or intrauterine growth retardation (IUGR) associated with essential fatty acid (DHA) and vitamin B12 intake or status observed in the Indian sub-continent also requires further examination.

In Egypt many nursing researches are carried out to examine the effect of iron deficiency anemia on pregnancy outcomes but there are scanty available researches that examine the effect of omega-3 Docosahexaenoic acid (DHA) supplementations to anemic pregnant women on the neonatal birth weight.

Therefore, this study will contribute to knowledge and practice on (DHA) supplementations and neonatal birth weight among anemic pregnant women. So, the current study aim to examine the effect of omega 3 (DHA) Supplementations on the neonatal birth weight among anemic pregnant women.



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Hypotheses:

H1: Anemic pregnant women who receive DHA Supplementations will experience lower rate of low birth weight than those who did not.

Subjects and methods

A Purposive sample of 240 anemic pregnant women divided into two groups 120 for each .Group (A) intervention group who received the DHA supplements (capsules and nutritional), Group (B) control group who received routine antenatal care. Both groups were followed-up until delivery of the neonates. Data was collected from control group first and then from the study group to avoid sample contamination. The sample was calculated by using power analysis¹⁰.

Inclusion criteria: women with singleton fetus between 24 and 30 weeks of gestation, primiparous and multiparous women (not more than 3 times), diagnosed with anemia (HB level from 9 g/dl to below 11g/dl) & on iron treatment and free from any other chronic diseases.

Exclusion criteria: Women who diagnosed with fetal congenital anomaly, on anticoagulant therapy, allergy to fish or fish products, current pregnancy complications, and any serious bleeding episode in the current pregnancy were excluded.

Data Collection Tools : Five Tools were used for data collection, Tools I, II, III were designed by the researcher and V, VI A dopted from WHO

I: Structured Interviewing Schedule. .

Which included Socio-demographic and obstetric profile and data related to current pregnancy.

II: Assessment and Follow up Tool.

Constituted based on baseline of body weight, height, to calculate body mass



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

index (BMI) according to international classification by scoring of (underweight : < 18.5, appropriate weight: 18.5 < 24.9, overweight: > 25-29.9, and obese : > 30)¹¹ ; blood pressure, HB level result , ultrasound for fetus, component of diet as the type, amount, and frequency of fish and fish products / week.

Follow up assessment included BMI, weight, BP, dangerous signs, occurrence of complications during pregnancy and compliance for DHA supplementations at each visit. Also, during ± 36 weeks gestation blood sample to assess women HB level and ultrasound to assess gestational age, auscultate FHR, assess fetal weight, amniotic fluid index, and observe for the absence of fetal congenital anomalies.

III: Nutritional Assessment Tool. .

This tool was designed based on perinatal Frequency Food Questionnaire (FFQ) (2013) to assess diet that included DHA supplements per week.

VI: Neonatal birth weight:

It was developed by WHO¹², to document neonatal weight after birth directly according to categories based on gestational age as (normal weight at term is 2500–4200 g; Low birth weight (LBW) is 2,499 g or less, Subcategories included very low birth weight (VLBW), which is less than 1500 g, and extremely low birth weight (ELBW), which is less than 1000 g , and high birth weight is more than 5000 g.

V: Gestational Age Assessment Chart (Tenth and ninetieth percentile)

It was developed by WHO¹³, it included assessment of the neonatal anthropometric measurements as weight, length, head circumference and plotted their results on the chart and compare them by using of curve at tenth and ninetieth percentile on the growth chart to determine if the neonate appropriate for gestational age (AGA), small for gestational age (SGA) or large for gestational



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

age (LGA) macrocosmic baby.

Procedure

An official permissions were obtained from the Hospital as well as written informed consent from women who met the inclusion criteria. The study was carried out on three phases: Interviewing and assessment , implementation, and follow-up phases.

(1) Interviewing and assessment phase:

Each woman in the study and control groups was interviewed for collecting data related to socio-demographic data and obstetric history, as well as history of previous pregnancies and deliveries; data were collected, individually and took around 15 minutes for each woman to be completed and recorded by the researcher. Assessment was performed for each woman in both groups during first meeting at 24th to 30th week of gestation to obtain the baseline data about the maternal anthropometric measurements such as Height, Weight, BMI, HB level results, ultrasound and dietary assessment.

(2) Implementation phase:

The nutritional protocol was applied to the study group at their first meeting during routine antenatal care follow-up visit through two steps. In the first step, the researchers was started to establish rapport with women, and then verbal instructions as a method of teaching was provided and supported with booklet about what is Omega -3 and DHA, diet rich in Omega -3 (DHA), how many grams (servings) that they should consumed per week, and importance of DHA for them and their fetuses. A total of 13hrs spent for Health educational that was held in a group of 3-5 women or individually as required. The second step included the administration of an oral supplement of omega- 3 fatty acid which was prescribed after permission from



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

outpatient clinic obstetrician to be taken orally two times per day after meals for 1000 mg fish oil capsules, each capsule contained 160 mg from DHA and completed with nutrition supplementation for 200 mg started from the 24th weeks of gestation till delivery provided by the researcher. The control group received routine- usual antenatal care.

Follow-up: All women in both groups were followed-up according to their scheduled antenatal care visits. The researcher followed-up and assessed each woman in relation to B.P, weight, and body mass index (BMI), dangerous signs, complications during pregnancy, components of diet per week. Also, the compliance of the women in the study group was assessed in each visit where the investigator asked women if their diet contained one nutrients of omega 3 daily in addition to one fish meal weekly. The women were followed-up by daily telephone calls and documented the women's response in the follow-up sheet and how many times missed taking capsules of DHA, if more than 3 times dropped from the study. Fortunately no woman was dropped from the study. All women in both groups were followed-up during labor to assess neonatal birth weight and neonatal anthropometric measurements as indicators of the effect of the DHA supplementations. Neonatal anthropometric measurements such as Length, weight, head circumferences was assessed by the researcher within 2 hours after delivery and plotted on growth chart to determine if the growth below 10th percentile, appropriate, or above the 90th percentile.

Results:

Results revealed that 48.3% of mothers in the study group as compared to 54.2% of mothers in the control group, their age range was between 25- 35 ; with mean age of 25 ± 4.7 in the study group as compared to 26 ± 5.3 in the control group, with no



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

statistical significant differences between them $p=0.37$. Twenty- eight point three percent of mothers in the study group as compared to 23.3% in the control group received preparatory education. Eighty-four point two percent & 85% of mothers in the study & control group respectively were house wife. While 48.3% of them in the study group as compared to 51.8% in the control group live in urban areas. There were no statistical significant differences between both groups.

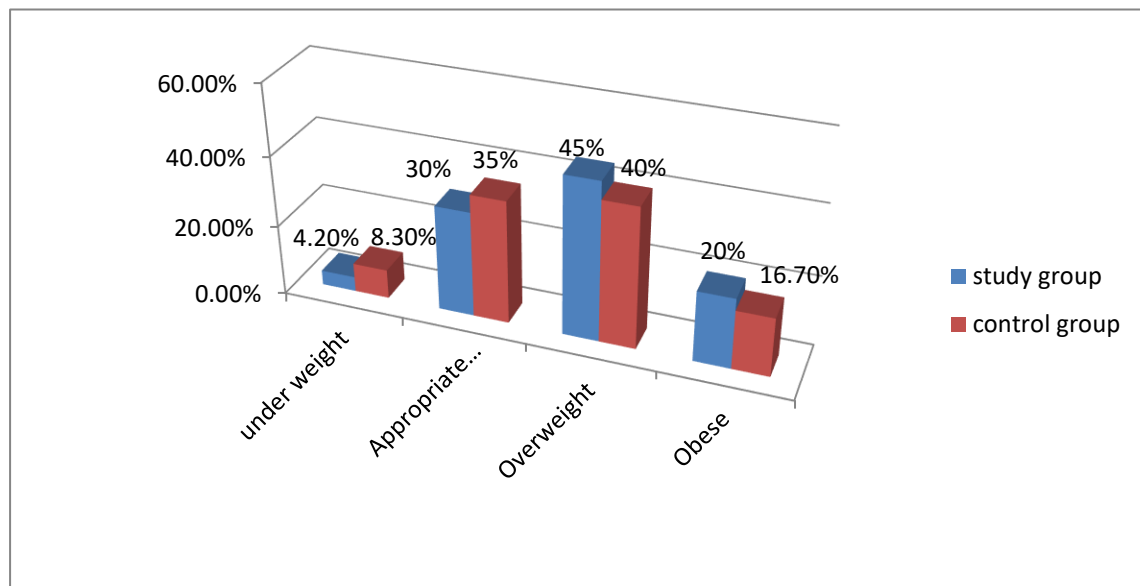
Results showed that 32.7% of mothers in the study group as compared to 35.6 % of mothers in the control group experienced previous complications such as anemia (31.3%&21.6% respectively); fetal distress (15.6%&10.8%respectively) and, Postpartum bleeding (12.5%&16.2% respectively). There were no statistical significant differences between both groups.

Findings of this study showed that Mean body weight of mothers in the study group was (70.57 ± 11.2) as compared to (66.85 ± 10.9) in the control group. There was no statistical significant difference between both groups $p=0.27$. Mean height of mothers in the study group was (161.33 ± 5.14) as compared to (163.55 ± 4.96) in the control group, there was no statistical significant difference between both groups . Fig. (1) reveals that 45% of mothers in the study group as compared to 40% of them in the control group had an overweight their BMI was (25 – 29.9) with mean BMI 24.9 ± 3.7 in the study group as compared to 24.51 ± 3.56 in the control group with no statistical significant differences between both groups ($p=0.97$).



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Fig (1) Distribution of Mothers Among Both Groups by Their BMI Classifications



Nerveless, 16.7% of mothers in the study group as compared to 25.8% in the control group their diet contained DHA in their nutrition. The mean HB level of mothers on admission was 10.07 ± 0.38 in the study group as compared to 10.1 ± 0.38 in the control group with no statistical significant differences between both groups ($p=0.54$), While, the mean HB level of mother at ± 36 wks gestation after DHA intervention was 10.88 ± 0.38 in the study group as compared to 10.39 ± 0.24 in the control group with significant difference between groups at $p\text{-value} = 0.0001$.

Table (1) Shows that mean fetal weight by US on admission in the study group was 1676.76 ± 240.2 as compared to 1651.5 ± 230.9 in the control group with no statistically significant difference between both groups $P= (0.51)$. While, at ± 36 wks gestation the mean fetal weight was higher in the study group than in the control group, it was (2955 ± 284.19 , & 2645.75 ± 308.31 respectively), with statistically significant difference between both groups at ($p = 0.0001$).



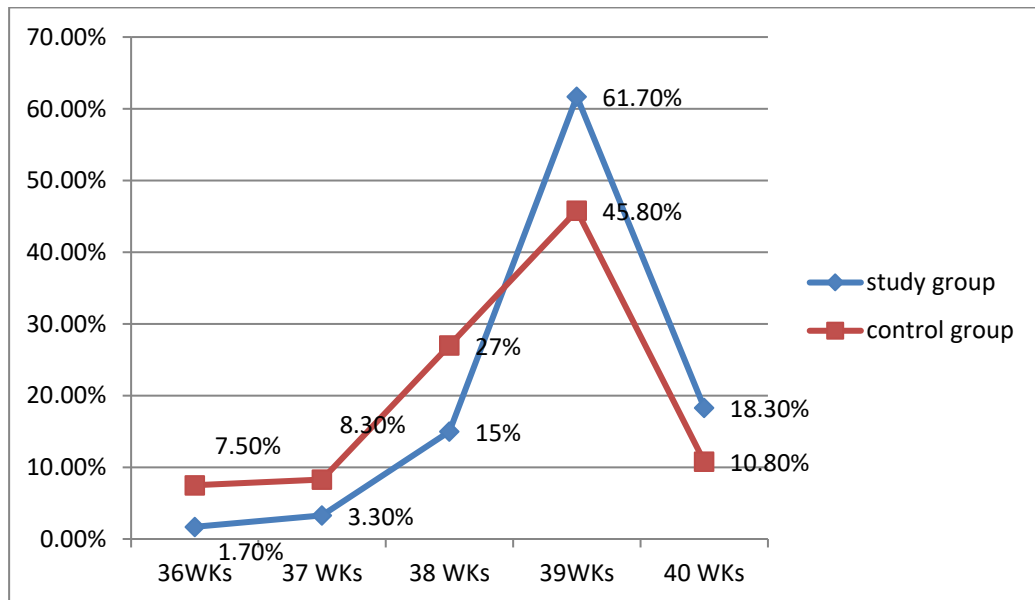
EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Table (1): Distribution of mothers in both groups by their Mean fetal Weight on Admission and 36 wks during Pregnancy by ultrasound

Items	Study group			Control group			t-value	p-value
	Total No	Mean	±SD	Total No	Mean	±SD		
Fetal Wt by US on Admission	120	1676.76	240.2	120	1651.5	230.9	0.42	0.51
Fetal Wt at 36wks	120	2955	284.19	120	2645.75	308.31	7.866	0.0001*

Fig (2) shows that, 1.7% of mothers in the study group as compared to 7.5% in the control group delivered neonates at + 36wks of gestation, while, 61.7% of mothers in the study group as compared to 45.8% in the control group delivered neonates at ±39 wks of gestation, There was statistical significant differences between both groups at p-value = 0.0001.

Fig (2) Distribution of Mothers in both groups by their neonatal GA at Time of Delivery (N=120)



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

Table (3) illustrates that 85.8% of mothers in the study group as compared to 75 % in the control group their neonates had weight range was between 2500-3500 weight, with mean neonatal weight 2608.3 ± 459.1 in the study group as compared to 2375 ± 219.4 in the control group with a highly statistically significant differences between both groups $P = 0.0001$. Also, mean neonatal length was 49.5 ± 1.3 in the study group as compared to 48.8 ± 1.8 in the control group, with statistical significant differences between both groups at p -value = 0.002. While, mean chest circumference was 31.96 ± 0.68 in the study group as compared to 31.5 ± 0.89 in the control group, with statistical significant differences between both groups at p -value = 0.0001. Mean head circumference was 33.82 ± 0.54 in the study group as compared to 33.34 ± 1.14 in the control group, with statistical significant differences between both groups at p -value = 0.0001.

Table (3): Distribution of Mothers in both groups by their Neonatal anthropometric measurements ($N = 120$).

Items	Study group (n = 120)		Control group (n = 120)		T	p-value
	No	%	No	%		
Neonatal weight						
2000-	7	5.8	30	25	11.6	0.0001
2500-	103	85.8	90	75		
>3500	10	8.4	0	0		
Mean \pm SD	2608.3 \pm 459.1		2375 \pm 219.4			
Neonatal length						
40	9	7.5	22	18.3	3.19	0.002
\leq 52	111	92.5	98	81.7		
Mean \pm SD	49.5 \pm 1.3		48.8 \pm 1.8			
Chest circumference						
29	0	0	7	5.8	4.001	0.0001
\leq 33	120	100	103	85.8		
Mean \pm SD	31.96 \pm 0.68		31.50.89			
Head circumference						



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

30	4	3.3	21	17.5	4.09	0.0001
≤35	116	96.7	99	82.5		
Mean ±SD	33.82	±0.54	33.34	±1.41		

Table (4) shows that 83.3% of mothers in the study group as compared to 78.3% in the control group delivered neonates appropriate for gestational age, while 8.3% of mothers in the study group as compared to 21.7% in the control group delivered neonates small for gestational age with statistical significant differences between both groups at p-value = 0.0001.

Table (4): Distribution of Mothers in both groups by their Neonatal Gestational Age

Assessment Chart (N =120).

Items	Study group (n = 120)		Control group (n = 120)		x ²	p-value
	No	%	No	%		
Neonatal Gestational Age Assessment Chart (Tenth and ninetieth percentile)						
Small for gestational age	10	8.3	26	21.7	21.1	0.0001
Appropriate for gestational age	100	83.3	94	78.3		
Large for gestational age	10	8.3	0	0		

Discussion

Many studies have demonstrated a link between maternal fatty acids (FAs) intake and pregnancy outcomes, including neonate's birth weight and birth length. Despite these findings, the mechanisms underlying the correlation between maternal FAs intake and fetal size have not been fully elucidated. Nevertheless, deficiencies in the levels of the mothers' FAs intake could have negative outcomes on the birth weight, birth length, and gestational age of the infant, as fetal development is entirely



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

dependent on the maternal supply of essential FAs¹⁴. Long-chain polyunsaturated fatty acids (LCPUFAs), such as docosahexaenoic acid (DHA; 22:6 n-3) and arachidonic acid (ARA; 20:4 n6), are important for the development of the fetus during pregnancy¹⁵. Omega-3 FAs have received considerable attention in exploring the correlations of maternal FAs intake with birth weight. Several studies have indicated that gestational age, birth weight, and birth length increase when the consumption of omega-3 FAs during pregnancy increases. However, other studies have shown conflicting results¹⁵. Fetal growth requires the presence of a normal placental function and an adequate maternal nutritional status. Low birth weight (LBW) is associated with short and long term morbidity and mortality.

The aim of this study was to examine the effect of omega-3(DHA) supplementations on the neonatal birth weight among anemic pregnant women.

The results of this study will be discussed within the following frame of reference: Effect of omega-3(DHA) supplementations on the neonatal birth weight among anemic pregnant women. Findings of this study supported the research hypothesis that anemic pregnant women who receive DHA Supplementations will experience lower rate of low birth weight than those who did not.

Several studies reported the effect of DHA supplementation on newborn weight. Regarding neonatal GA, and anthropometric measurements, the findings of the current study revealed a highly significant statistical difference between both groups related to the length of gestational age. That two-third mother in the study group had neonates with a higher gestational age than neonates in the control group. These results are in harmony with a study done to test the effect of vaginally administered DHA versus placebo on 43 women at high risk for preterm delivery. The supplemented group had a



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

significant increase in gestational age at delivery and in newborn birth weight. Also, the study results were consistent with a more recent systematic review and meta-analysis of 9 RCTs studies conducted on the preventive role of omega-3 supplementation in asymptomatic singleton pregnancies with a previous history of preterm labor, was not conclusive for a beneficial effect on the outcome. Supplemented group and controls had similar incidence of preterm labor and secondary neonatal outcome. However, in the omega-3 treated group, there was a significant longer latency and higher birth weight suggesting a possible benefit of the supplementation¹⁶. In Addition, a double blind RCT study conducted on 350 women receiving either 600mg/d DHA or placebo, the study reported that supplementation during the last half of gestation resulted in overall greater gestation duration and infant size¹⁷. Same results have shown from study on n_3 LC-PUFA supplementation given during pregnancy finding that increase in duration of pregnancy by an average of 1.6d, at time of birth¹⁸. Also In RCT study on effect supplementation with fish oil during pregnancy that shows significantly increase in duration of pregnancy (2.77 days) and significantly birth weight (97g; 95% CI: 8,186g¹⁹).

These results contradicted with a double-blind RCT study conducted on 1094 pregnant women who received (400 mg DHA versus placebo) did not show any difference in the mean gestational age, weight and head circumference between the 2 groups²⁰. these contraindications in the findings among studies may be due to differences in sample characteristics as parity, time of administration for DHA , dose & Rote.

Findings of the current study revealed a highly statistically significant difference between both groups related to the neonatal anthropometric measurement as



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

mean birth weight & mean head circumference in the two groups. Mean neonatal birth weight was 2608.3 ± 459.1 in the study group as compared to 2375 ± 219.4 in the control group ($P = 0.0001$) and Mean head circumference was 33.82 ± 0.54 in the study group as compared to 33.34 ± 1.14 in the control group ($p = 0.000$). Overall, the findings agree with the randomized trials study showed that a consumption of fish oil in pregnancy can increase birth weight by prolonging gestation and reduce the risk of recurrence of preterm delivery²¹. In the same context, the study results are consistent with a systematic review and meta-analysis study conducted on the benefits of n-3 fatty acids demonstrated that women with n-3 fatty acids supplementation delivered neonates with mean birth weight was higher than those in control group²² and an observational study conducted on women consumed fish and received an additional supplementation of 200 mg DHA /day showed that they have a lower incidence of preterm labor and an increased neonatal weight as compared to control group without supplementation²³. Moreover, the prospective study conducted on pregnant women in the first trimester supplemented with DHA and their DHA concentration level in maternal erythrocytes was significantly correlated with neonatal weight as compared to women in control group who had lower DHA levels were delivered low birth weight infants.²⁴

Also, the study conducted on pregnant women in the second trimester revealed that fish oil containing 2.7 g omega-3 fatty acids (EPA DHA)/day from 30th week of pregnancy until parturition produced the most significant increase in infant weight at birth by 107 g, while consuming DHA (33 or 133 mg) from eggs at 24th and 28th week of pregnancy until parturition increased gestation length the most by 6.0 ± 2.3 days ($P \frac{1}{4} 0.009$) in the higher DHA group²⁵.

Addition, the study conducted on 400 pregnant women who received algal DHA & olive oil the study revealed that babies born of primiparous Mexican women



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

who received 400 mg/d of algal DHA during the second half of the pregnancy term were heavier and had larger head circumferences at birth than children whose mothers received placebo (olive oil). However, no effect was observed in multiparous mothers. Children of primiparous women who were given DHA were taller at 18 months than those of primiparous women given placebo²⁶. May be due to primiparous women were, on average, younger than the multiparous women, their own body stores of DHA are not well established and available to the fetus and infant and type and time of intervention .

On the other hand, study conducted to assess effect of omega-3 fatty acids supplementation during pregnancy for women at high risk of preterm birth, the study reported that there was no effect of omega 3 on the prevention of preterm birth, pre-eclampsia, IUGR or increasing birth weight²⁷.

Also, these results contradicted with a prospective, observational cohort study conducted on 2109 mothers to investigate if maternal marine n-3 LCPUFAs and seafood intake were associated with birth weight, length of gestation, low birth weight, preterm delivery, and babies' small for gestational age. They found the increased consumption of the n-3 LCPUFAs DHA and EPA was associated with a modest decrease in fetal growth. The study did not show any association between higher seafood or n-3 LCPUFAs intake and length of gestation²⁸. And a prospective study conducted on 62099 women to investigate the influence of maternal intakes of seafood and supplementary n-3 LCPUFAs in infant birth weight, length, and head circumference. The study found that maternal seafood consumption was positively associated with birth size, driven by lean fish intake, while supplementary n-3 intake was negatively associated with infant head circumference²⁹.the contraindications in the



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

findings may be due to differences in sample characteristics as parity, high risk group, and time of administration for DHA, dose, route & type of DHA supplement.

In relation to neonatal Gestational Age Assessment Chart (Tenth and ninetieth percentile), the findings of the current study revealed that There was statistical significant differences between both groups at $p\text{-value} = 0.0001$. these findings are in accordance with the Evidence Report/Technology Assessment on Omega-3 Fatty Acids and Maternal and Child Health: An Updated Systematic Review which prepared by Agency for Healthcare Research and Quality 2016 which concluded that found a significant effect of maternal n-3FA supplementation on the risk for low birth weight (LBW) or small-for-gestational age, (SGA) birth or a clear association of any maternal biomarkers with risk for low birth weight or birth weight itself. For the current report, authors found a moderate level of evidence that maternal supplementation with DHA may increase birth weight and a low level of evidence that maternal supplementation with EPA+DHA may not have significant effects on birth weight compared with placebo. Twelve RCTs studies showed significantly higher birth weights among infants (mixed term and preterm) whose mothers received algal DHA. Also, the findings of the current study are consistent with prospective observational studies, which found that higher maternal blood DHA concentrations were associated with higher birth weight.³⁰

Conclusion:

In conclusion, gestational age, birth weight, and neonatal length were increased when the consumption of omega-3 FAs during pregnancy also increased. So the research hypothesis was accepted.



EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

The study recommended the following:

- raise awareness of anemic pregnant women who had previous low birth weight in antenatal clinic regarding the importance of higher n-3 FAs intake during pregnancy to reduce the occurrence of low birth weight
- Further RCTs & systematic review researches exploring the effect of n-3 FAs intake during pregnancy on the occurrence of low birth weight.

Ethical clearance

A Written approval was obtained from the Research Ethics Committee of the Faculty of Nursing Cairo University. Written informed consent was obtained from each participant after explaining the nature & purpose of the study. Participants were informed that participation in the study was entirely voluntary, anonymity and confidentiality of the data were assured.

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Conflict of interest: The authors declare that there is no conflict of interest.



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EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

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EFFECT OF (DHA) SUPPLEMENTATIONS ON THE NEONATAL BIRTH WEIGHT

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