Prostaglandins, Leukotrienes and Essential Fatty Acids 177 (2022) 102398

Contents lists available at ScienceDirect

Prostaglandins, Leukotrienes and Essential Fatty Acids

journal homepage: www.elsevier.com/locate/plefa

Original research article

Validation of an abbreviated food frequency questionnaire for estimating DHA intake of pregnant women in the United States

SA Crawford [a], DN Christifano [a,b], EH Kerling [a], BJ Gajewski [c], CJ Valentine [d], KM Gustafson [b], NB Mathis [b], JT Camargo [a], HD Gibbs [a], DK Sullivan [a], SA Sands [a], SE Carlson [a,*]

[a] The University of Kansas Medical Center, Department of Dietetics and Nutrition, Kansas City, KS, United States of America
[b] The University of Kansas Medical Center, Hoglund Biomedical Imaging Center, Kansas City, KS, United States of America
[c] The University of Kansas Medical Center, Department of Biostatistics & Data Science, Kansas City, KS, United States of America
[d] Banner University Medical Center, The University of Arizona, Department of Pediatrics, Tucson, AZ, United States of America

ARTICLE INFO

Keywords:
DHA
Food frequency questionnaire
Omega-3
Polyunsaturated fatty acid
Pregnancy
Validation

ABSTRACT

Docosahexaenoic acid (DHA) intake was estimated in pregnant women between 12- and 20-weeks' gestation using the National Cancer Institute's (NCI) Diet History Questionnaire-II (DHQ-II) and a 7-question screener designed to capture DHA intake (DHA Food Frequency Questionnaire, DHA-FFQ). Results from both methods were compared to red blood cell phospholipid DHA (RBC-DHA) weight percent of total fatty acids. DHA intake from the DHA-FFQ was more highly correlated with RBC-DHA (r_s=0.528) than the DHQ-II (r_s=0.352). Moreover, the DHA-FFQ allowed us to obtain reliable intake data from 1355 of 1400 participants. The DHQ-II provided reliable intake for only 847 of 1400, because many participants only partially completed it and it was not validated for Hispanic participants. Maternal age, parity, and socioeconomic status (SES) were also significant predictors of RBC-DHA. When included with estimated intake from the DHA-FFQ, the model accounted for 36% of the variation in RBC-DHA.

Abbreviations

ADORE	Assessment of DHA on Reducing Early preterm birth
DHA	Docosahexaenoic acid
DHA-FFQ	DHA Food frequency questionnaire
DHQ-II	Diet History Questionnaire-II
EPA	Eicosapentaenoic acid
FFQ	Food frequency questionnaire
NCI	National Cancer Institute
n-3	Omega-3
PANDA	Prenatal Autonomic Neurodevelopmental Assessment
PUFA	Polyunsaturated fatty acid
RBC	Red blood cell
SES	Socioeconomic status
USA	United States of America
USDA	United States Department of Agriculture

1. Introduction

Consumption of the omega-3 (n-3) long-chain polyunsaturated fatty acid (PUFA) docosahexaenoic acid (DHA) in pregnancy can be advantageous for both mom and baby. Reported benefits of prenatal DHA or DHA and eicosapentaenoic acid (EPA) supplementation include reduced risk of preterm (<37 weeks gestation) and early preterm birth (< 34 weeks gestation) [1, 2], a positive influence on offspring brain development [3] and body composition [4–7], and a reduced risk of asthma in offspring [8, 9].

Clinical research requires a valid indicator of participants' DHA status at baseline and study completion [10]. This is typically done by measuring red blood cell (RBC), plasma or blood spot DHA as a percent of total fatty acids [11]. An indirect method for assessing DHA status is to use one of several tools that evaluate the DHA content of foods consumed. In addition to dietary intake of DHA, other factors such as age [12], genetics [8], and parity [13] are associated with blood levels of DHA.

Currently, there is no food frequency questionnaire (FFQ) that has

* Corresponding author at: Department of Dietetics and Nutrition, MS 4013, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160 United States of America
E-mail address: scarlson@kumc.edu (S. Carlson).

https://doi.org/10.1016/j.plefa.2022.102398
Received 29 September 2021; Received in revised form 3 January 2022; Accepted 6 January 2022
Available online 13 January 2022

been validated to assess DHA intake in pregnant women in the United States of America (USA) [14]. Questionnaires exist in other countries as either abbreviated PUFA FFQs [15, 16] or complete FFQs, sometimes modified with additional questions regarding n-3 rich foods and supplements [17–20]. However, since diet is extremely reflective of regional culture, a questionnaire must be validated in a representative sample of the target population [21, 22].

The primary goal of the present study was to compare RBC-DHA to DHA dietary intake assessed at baseline in two large clinical trials of DHA supplementation in pregnancy. We used both the National Cancer Institute's (NCI) Diet History Questionnaire-II (DHQ-II) [23] and a 7-question FFQ designed specifically to estimate DHA intake (DHA-FFQ) [24]. The 7-question FFQ was validated as an interviewer-administered questionnaire in a healthy US adult population [24], but its application in a pregnant population has not previously been evaluated. A secondary aim of this study was to identify maternal characteristics other than dietary intake that predicted RBC-DHA status in this population.

2. Methods

2.1. Participants

The data analyzed were gathered at baseline from two National Institute of Child Health and Human Development (NICHD) supported randomized clinical trials: The Assessment of DHA on Reducing Early Preterm Birth (ADORE) multi-site trial [25] and the Prenatal Autonomic Neuro-Developmental Assessment (PANDA) study. Both studies were registered with ClinicalTrials.gov (ADORE: NCT02626299; PANDA: NCT02709239). All subjects provided written consent prior to the occurrence of any study activities.

Subjects included 1400 women age 18 or older with a singleton pregnancy who could read and speak either English or Spanish. All participants attended a baseline study visit between 12- and 20-weeks' gestation at which they were administered the DHA-FFQ and had a blood sample collected. In the PANDA study, all women spoke English and were asked to complete the DHQ-II, regardless of race and ethnicity. The inclusion of Spanish-speaking women in the ADORE trial provided a high number of Hispanic participants in the sample. However because the DHQ-II is not validated for Hispanic persons [26], those in the ADORE trial were not asked to complete the DHQ-II ($N = 207$). Measures of socioeconomic status (SES) were available from the primary trials including maternal education, paternal education, annual household income, insurance type, and marital status.

There were 1400 enrollments and baseline visits in the two clinical trials. Thirty-two enrollments were excluded from this study. Exclusions included nineteen women who participated in both trials with subsequent pregnancies. In these cases, only data from the first trial in which they participated were included. Ten enrollments were excluded because the baseline blood sample was missed or damaged, and three participants were excluded because they did not complete either the DHA-FFQ or DHQ-II. Thirteen participants who were included completed the DHQ-II but did not have a valid DHA-FFQ.

2.2. DHA food frequency questionnaire (DHA-FFQ)

The DHA-FFQ was developed by Martek Biosciences Corporation (now DSM Nutritional Products) to assess dietary intake of DHA-rich foods and supplements consumed in the past two months [24]. The questionnaire consists of seven questions and was administered by a trained interviewer at the baseline study visit. Serving size is specified as 3 ounces for all questions, except egg yolks. A deck of playing cards was used as a visual representation of a 3-ounce serving. The first three questions ask about fish and seafood intake in three categories that vary in DHA content: high, medium, or low DHA. Each question lists species of fish and asks for the number of 3-ounce servings consumed monthly. Question four asks for the number of 3-ounce serving of liver consumed monthly. Questions five and six assess weekly intake of egg yolks and 3-ounce servings of poultry, respectively. The seventh question asks about DHA-containing dietary supplements and functional foods. Detailed information was obtained for dietary supplements and functional foods containing DHA, including brand name and label when available, the dose or serving size consumed, number of days per week it was consumed, and when the participant started and/or stopped using the supplement or food.

For the first six questions, the number of servings reported (per month for questions 1–4; per week for questions 5–6) is multiplied by a prespecified factor based on mean DHA content of each item from the United States Department of Agriculture (USDA) Nutrient Database (USDA, Nutrient Database for Standard Reference release 14, 2002) [24, 27]. The product of each question is added together to give an approximation of DHA consumed in mg per day. Information collected about supplements and functional foods containing DHA is then added to estimate total daily DHA intake in mg per day [24].

Kuratko [24] validated the DHA-FFQ in a sample of 67 healthy adults. DHA intake estimated by the DHA-FFQ was correlated with both RBC-DHA and plasma phospholipid DHA ($r = 0.513$ and $r = 0.514$, respectively). There was also no significant difference between intake from the DHA-FFQ and intake estimated by computerized analysis of a 14-d diet record, therefore confirming content reliability. Additionally, the 7-question FFQ has previously been used in two clinical trials. Using the DHA-FFQ to calculate intake, DHA intake of older adults was compared to plasma phospholipid DHA and intake of preschool children was compared to whole blood DHA. Both studies found significant, moderate correlations between DHA intake and the biomarker used (older adults: $r = 0.59$; children $r = 0.55$) [28, 29].

For the ADORE trial, the DHA-FFQ was translated to Spanish using a systematic approach of both linguistic and cultural comparison of food (checking face validity for Hispanics). It was administered by a team member fluent in Spanish for women who preferred to complete the questionnaire in Spanish.

2.3. Diet history questionnaire-ii (DHQ-II)

In addition to the DHA-FFQ, all PANDA subjects and non-Hispanic ADORE subjects completed the electronic version of the NCI's DHQ-II at their baseline study visit. The DHQ-II is a complete FFQ that was developed by the Risk Factor Assessment Branch of the NCI's Epidemiology and Genomics Research Program. It has been validated as a means to assess overall dietary intake [30, 31] and is freely available for use in research. The DHQ-II consists of 134 items. The standard format was used, which asks about diet over the past year and includes questions about portion size [23, 32]. Questionnaires were analyzed using the Nutrient and Food Group Database [33] and Diet*Calc software [34], both of which can be downloaded from the NCI website [35, 36].

2.4. Red blood cell phospholipid concentration

At the baseline visit, a blood sample was collected by venipuncture and immediately placed on ice. Samples were centrifuged within 24 h to separate plasma, buffy coat, and anticoagulated RBCs, and these fractions were stored at -80 °C. RBC lipids were extracted, RBC phospholipids separated by thin layer chromatography, fatty acids transmethylated with boron trifluoride methanol and the resulting fatty acid methyl esters separated by gas chromatography at the University of Kansas Medical Center as previously reported, with DHA reported as weight percent of total RBC phospholipid fatty acids (RBC-DHA) [1, 25].

2.5. Statistical analysis

All analyses were performed using IBM SPSS Statistics for Windows (Version 26.0). Level of significance was set at $p < 0.05$ and 95% CI. General descriptive statistics were used to describe population

characteristics.

Preliminary testing for normality was done using histograms and the Shapiro-Wilk test. The three primary outcome variables: RBC-DHA, DHA intake from the DHA-FFQ, and DHA intake from the DHQ-II all showed asymmetric distributions. Because of the skewed distributions, Spearman's rank correlation was used to evaluate all relationships [37, 38]. However, both Pearson's and Spearman's were tested, and the correlations were similar. To further support the findings, 95% CI were also calculated to accompany each of the correlations [37]. Linear regression was used to evaluate the role of RBC-DHA predictors, other than dietary intake (see Section 3.2).

3. Results

A detailed description of the population can be found in Table 1.

3.1. Primary outcome variables

DHA intake estimated by the DHA-FFQ had a good correlation with RBC-DHA (n = 1355, r_s=0.528; 95% CI: 0.49–0.57) (Table 2). This relationship is illustrated in Fig. 1. However, the correlation between DHA intake estimated by the DHQ-II and RBC-DHA was only acceptable (n = 847, r_s=0.352; 95% CI: 0.29–0.41) (Table 2). Not only was the DHA-FFQ superior to the DHQ-II for predicting RBC-DHA, but it also captured DHA intake from 97% of participants. In contrast, the DHQ-II only provided estimated intake of 60% of participants. The DHQ-II was also poor for predicting DHA intake from supplements and DHA-containing food products, resulting in an underestimation of DHA intake compared to the DHA-FFQ.

Table 1
Subject Characteristics.

Characteristics	N (%) or Mean ± SD
Study – Site	N = 1368
ADORE – KUMC	470 (34.36)
ADORE – OSU	355 (25.95)
ADORE – UC	251 (18.35)
PANDA – KUMC	292 (21.35)
DHA-FFQ Only (no DHQ-II)	521 (38.10)
DHQ-II Only (no DHA-FFQ)	13 (<1)
Both DHA-FFQ and DHQ-II Valid	834 (60.96)
RBC DHA (%)	6.49 ± 1.78
DHA-FFQ – TOTAL DHA INTAKE (mg/d)	153.52 ± 117.69
DHQ-II – TOTAL DIETARY DHA INTAKE (mg/d)	65.11 ± 71.1
Maternal Age (years)	30.16 ± 5.47
Parity (number)	1.13 ± 1.36
GA at Enrollment	16.83 ± 2.47
Father of Baby Education (years)	14.25 ± 3.09
Mother of Baby Education (years)	14.67 ± 3.07
Preferred Language	
English	1210 (88.45)
Spanish	158 (11.55)
Maternal Race or Ethnicity	
American Indian or Alaskan Native	6 (0.44)
Asian	38 (2.78)
Biracial: Asian, White	9 (0.66)
Biracial: Black, Asian	1 (0.07)
Biracial: Black, White	14 (1.02)
Biracial: Native American, White	1 (0.07)
Black or African American	273 (19.96)
Hispanic	278 (20.32)
Multiracial: Black, Asian, White	1 (0.07)
Multiracial: Black, Native American, White	4 (0.29)
Native Hawaiian or other Pacific Islander	2 (0.15)
Other [1]	6 (0.44)
White	735 (53.73)
Taking a DHA-Containing Supplement at Baseline	
Yes, DHA Supplement	705 (51.54)
<200 mg/day	270 (38.30)
≥200 mg/day	435 (61.70)
No, DHA Supplement	663 (48.46)

ADORE, The Assessment of DHA on Reducing Early Preterm Birth. KUMC, The University of Kansas Medical Center. OSU, The Ohio State University Medical Center. UC, The University of Cincinnati Medical Center. PANDA, Prenatal Autonomic Neuro-Developmental Assessment. RBC, Red blood cell. DHA, Docosahexaenoic acid. FFQ, Food frequency questionnaire. DHQ-II, Diet history questionnaire-II. GA, Gestational age.

[1] "Black & Indian", "Arab", "Arab, White", "Asian-Pakistani", "Middle Eastern".

Table 2
Correlations between predictor variables and RBC-DHA.

		Spearman's Rho		
	n	r_s	95% CI	p-value
DHA-FFQ	1355	0.528	0.486, 0.568	0.000
DHQ-II	847	0.352	0.290, 0.411	0.000
Maternal Age	1368	0.250	0.199, 0.300	0.000
Parity	1366	-0.212	-0.263, -0.160	0.000
Father of Baby Education	1321	0.461	0.415, 0.505	0.000

3.2. Secondary outcome variables

Alone, the DHA-FFQ accounted for 27% (r^2=0.268) of the variance in RBC-DHA. Several measures of socioeconomic status (SES) were tested for their role in predicting RBC-DHA status including maternal education, paternal education, annual household income, insurance type, and marital status. Paternal education was collinear with income (r_s=0.686) and included as the sole measure of SES. Other significant predictive factors were maternal age and parity. The final multivariable linear regression model included RBC-DHA as the dependent variable and the following independent variables: DHA intake estimated by the DHA-FFQ, maternal age, parity and paternal education. These four predictors accounted for 36% of the variation in RBC-DHA (r^2=0.360) (Table 3).

4. Discussion and conclusions

The DHA-FFQ was more highly correlated with RBC-DHA than the DHQ-II. The DHA-FFQ also identified a higher mean DHA intake at baseline. This is likely because many participants in this study of DHA in pregnancy were consuming a prenatal supplement that contained DHA, which was captured by the DHA-FFQ and poorly captured by the DHQ-II. Another important advantage of the DHA-FFQ was that it allowed us to estimate DHA intake at baseline in 97% of the participants who enrolled in the two randomized clinical trials.

Mother's age, parity and years of father's education further increased the ability to predict RBC-DHA. Mother's age and years of father's education were both positively related to RBC-DHA while parity was negatively related. We don't have an explanation for these relationships although both positive predictors are related to higher socioeconomic status, which could be linked to a higher quality diet or reduced stress. Recent systematic reviews are in agreement about sociodemographic characteristics [39] and parity [40] on maternal DHA status, but both acknowledge that these factors cannot be fully explained.

To assess the quality of a dietary intake tool, Ortiz-Andrellucchi et al. [41] describes a correlation <0.30 as *poor*, between 0.30 and 0.50 as *acceptable*, between 0.51 and 0.70 as *good*, and >0.70 as *very good*. Based on these guidelines, the DHA-FFQ is a *good* tool for assessing intake of DHA in this population and the DHQ-II is only acceptable. The present study also identified several other factors that influence RBC-DHA level including age, parity, and SES.

These results are consistent with others who have validated abbreviated FFQs for estimating DHA or n-3 PUFA intake. In Australian pregnant women, Parker et al. [16] reported a good correlation between estimated DHA intake from a 38-item PUFA FFQ and RBC-DHA (r_s=0.61). Similar 20–30-item abbreviated FFQs have been validated in non-pregnant adult populations in several different countries with correlations between estimated DHA intake and RBC-DHA ranging from acceptable (r_s=0.39 in Australian adults [42] and r_s=0.40 in Canadian

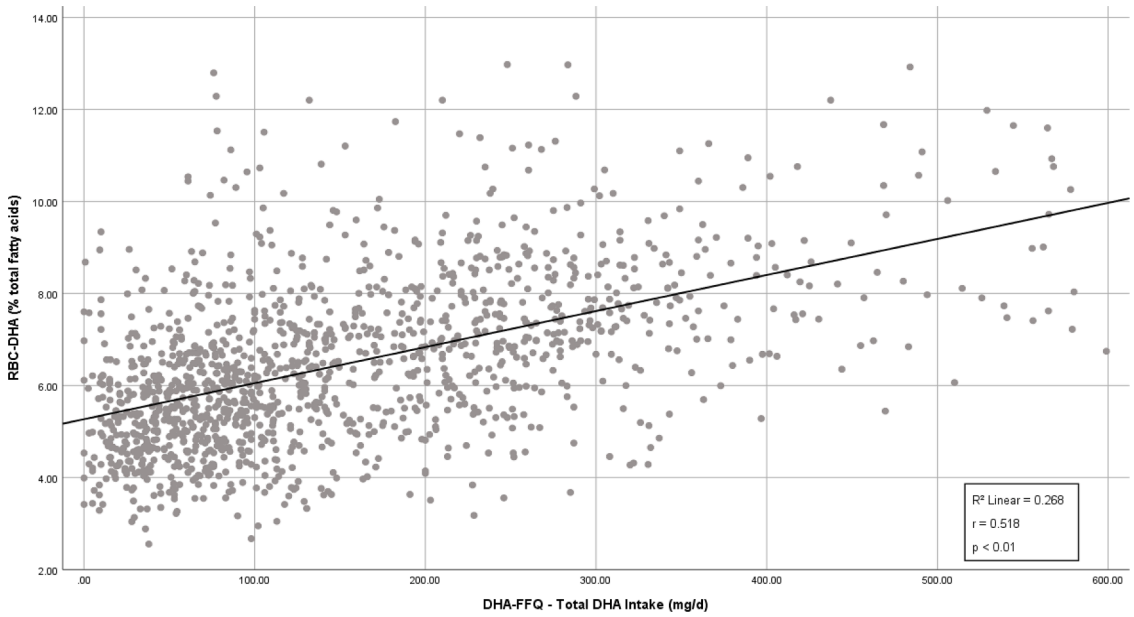

Fig. 1. Pearson's correlation between RBC-DHA & DHA-FFQ.

Table 3
Univariate and multiple linear regression models with RBC-DHA (% of total fatty acids) as the dependent variable and potential predictors of RBC-DHA as independent variables.

Predictor	Unstandardized B [1] (95% CI)	Beta	p-value	R^2	Unstandardized B [1] (95% CI)	Beta	p-value	Unstandardized B [1] (95% CI)	Beta	p-value
	Univariable Analysis				Multivariable Analysis DHA Intake - DHA-FFQ [2]			Multivariable Analysis DHA Intake - DHQ-II [3]		
DHA Intake - DHA FFQ (mg/d)	0.008 (0.007, 0.009)	0.518	0.000	0.268	0.006 (0.005, 0.007)	0.403	0.000			
DHA Intake - DHQ-II (mg/d)	0.007 (0.005, 0.009)	0.273	0.000	0.075				0.005 (0.003, 0.006)	0.184	0.000
Age at Enroll (years)	0.08 (0.064, 0.097)	0.246	0.000	0.061	0.032 (0.016, 0.048)	0.098	0.000	0.046 (0.022, 0.070)	0.132	0.000
Parity (each)	-0.256 (-0.324, -0.188)	-0.195	0.000	0.038	-0.098 (-0.164, -0.032)	-0.074	0.003	-0.125 (-0.224, -0.026)	-0.083	0.013
Father of Baby Education (years)	0.254 (0.226, 0.283)	0.439	0.000	0.193	0.146 (0.117, 0.176)	0.254	0.000	0.219 (0.172, 0.266)	0.321	0.000

[1] Percent increase in RBC-DHA for every one-unit increase (or decrease) of the predictor variable.
[2] Daily DHA intake estimated by the DHA FFQ. $R^2 = 0.360$.
[3] Daily DHA intake estimated by the DHQ-II. $R^2 = 0.233$.

adults with major depressive disorder [43]) to good (r_s=0.605 in Swiss adults [44]). In US adults, Sublette et al. [45] validated an accepTable 21-item n-3 fatty acid FFQ based on the correlation between estimated DHA intake and plasma DHA (r_s=0.50). With correlations >0.30, all of these instruments would be deemed acceptable, and those with correlations >0.51, like the DHA-FFQ, considered good [41].

As the results show, the DHA-FFQ is superior to the DHQ-II for to estimating DHA intake. The DHQ-II is designed to assess overall dietary intake with less focus on individual nutrients. It also asked about intake in the past 12 months while the DHA-FFQ assessed intake in the past 2 months. Because some women may change their diet in pregnancy, this could be another advantage of the DHA-FFQ in studies of pregnant women. Fish and seafood questions in the DHQ-II are grouped more by preparation method (fried vs. not-fried) while the DHA-FFQ categorizes fish and seafood based on their level of DHA. Furthermore, the DHQ-II does not incorporate DHA-containing supplements into its estimation. More than 50% of the study population was taking a DHA-containing supplement at baseline, as prenatal supplements with DHA in various amounts are readily available. Data from the National Health and Nutrition Survey show that the proportion of women taking a DHA supplement during pregnancy increased from 6% in the 2005–2006 cycle to 30% in 2015–2016 [46, 47] so there is clear evidence that DHA supplementation in pregnancy from the small number of pregnant women sampled yearly (n = 57 to 70) since 2006. DHA supplements are clearly a contributor to DHA intake; thus, it is critical to include them when estimating intake.

Others have also found that a tailored FFQ better estimates intake for specific nutrients compared to a complete FFQ. Meyer et al. [48] compared RBC-DHA to DHA intake estimated with a 38-item FFQ and found it better estimated DHA intake (validity coefficient=0.69) compared to a complete FFQ (validity coefficient=0.26). Similarly, Zhang et al. [49] found a slightly stronger correlation between a 21-item abbreviated FFQ and dried blood spot DHA (r_s=0.45) compared to the correlation between a complete FFQ and dried blood spot DHA

(r_s=0.40) in Australian adults.

Several validation studies have used a complete FFQ to estimate intake of DHA and other PUFAs in pregnant women. In Brazilian pregnant women, Lepsch et al. [18] found a significant correlation between DHA intake estimated by an 81-item complete FFQ and serum DHA concentration (r_s=0.209) and concluded that the FFQ could be used as a non-invasive method for predicting serum DHA and PUFA status. Similarly, Madsen et al. [19] reported a significant correlation between DHA intake estimated by a 360-item complete FFQ and plasma DHA concentration (r_s=0.18) in Danish pregnant women. In Japan, Shiraishi et al. [20] concluded that a 58-item brief-type, complete FFQ was an acceptable method for estimating DHA intake in pregnant women based on the correlation between estimated DHA intake and plasma DHA (r_s=0.305). Kobayashi et al. [17] evaluated the use of a 167-item complete FFQ for assessing PUFA intake in Japanese pregnant women and reported a significant correlation between estimated DHA intake and serum DHA level (r_s=0.27). While these studies and those previously mentioned [17, 42-45] found statistically significant correlations between estimated DHA intake and a biomarker of DHA status, just three others had a *good* correlation despite asking many more questions [16, 44, 48].

A strength of the present study is the use of a direct measurement of blood DHA as the reference method for validation. A biomarker is the preferred reference method for validating a dietary assessment method [50]. When using another method of dietary intake for validation, the same errors can occur in both instruments, potentially leading to a stronger than real correlation. Errors in measuring a biomarker are independent of the instrument being validated.

Another strength is the large and diverse sample size of 1400 subjects. Just over 50% of the sample population was Non-Hispanic white, with about 20% Non-Hispanic Black or African American and 20% Hispanic (Table 1). As noted previously, Hispanic women in the ADORE study were not asked to complete the DHQ-II. The DHA-FFQ however, was administered to all women in their preferred language, allowing for comparison of DHA intake across the entire sample. Additionally, a reasonable sample size for validation studies is estimated by Majem et al. [51] to be between 100 and 200 subjects but could be as low as 50 when a biomarker is used as the reference method. However, Coulston et al. [22] reports that a less precise instrument typically requires more individuals. Nevertheless, the sample size is sufficient for validation and representative of the midwestern US population.

There are some important limitations of the study to consider as well. All participants were living in the Midwest of the US when the study was conducted. According to the US Environmental Protection Agency [52], adults living in the Midwest, including Kansas, Missouri and Ohio, have the lowest estimated total fish intake compared to the three other US Census Bureau regions: the Northeast, South, and West. That said, the percentage of ADORE/PANDA participants who never consumed any fish/seafood (21.7%) is somewhat lower than the average from NHANES from 1999 to 2018 (25.9%) [53]. Seafood intake in pregnancy may also be increasing as efforts are being made to educate women that seafood can be a healthful dietary choice in pregnancy. Nevertheless, because patterns of fish and seafood intake may vary and influence the quality of nutrients being consumed from this food source, it may be desirable to validate the questionnaire in other populations.

Meyer [54] mentions limitations to the DHA-FFQ. For one, the questionnaire groups fish and seafood into only three categories, and there are variations in the amount of DHA of the fish within each category. This limitation is of less concern in a population that consumes little fish, such as the one we studied. It should also be noted that, variations in nutrient composition exist even within the same species of fish. For example, according to the USDA's Food Data Central [55], raw salmon can have between 333 mg and 1385 mg of DHA per 100 g. There are also known sources of error in any FFQ such as recall bias, under/-over reporting, and variations in usual intake [16, 22]. Therefore, even a more detailed abbreviated FFQ, such as one that has individual questions for each species of fish, cannot measure intake perfectly. Meyer [54] also mentions the exclusion of red meat on the DHA-FFQ as a limitation. However, red meat (beef, pork, and lamb) has an average of 0.6025 mg of DHA per 100 g according to the DHQ-II Nutrient Database [33]. An individual consuming six ounces of red meat per day would consume an additional 1.2 mg of DHA, which does not justify adding additional questions about red meat intake.

While the DHA-FFQ may not measure DHA intake precisely, it still has several strengths as an assessment instrument. Because many high-DHA foods like fish and seafood are not consumed on a regular basis, such an FFQ is advantageous since it is designed to assess intake over an extended period [56]. In the literature, an abbreviated or semi-quantitative FFQ, similar to the DHA-FFQ, that is targeted specifically to DHA or n-3 PUFAs is the most common tool used to assess dietary intake of DHA [2, 6, 16, 57]. With only seven questions, it takes approximately five minutes to complete, and the results are known immediately.

In conclusion, the DHA-FFQ is a good and valid instrument for estimating DHA intake in midwestern, US pregnant women. The short time required for administration and the ability to obtain data from virtually everyone make it ideal for use in research. Our results also support the importance of collecting information about socioeconomic status of participants.

Funding

This work was supported by grants from The National Institutes of Health Child Health and Human Development (NICHD) (ADORE: R01HD083292, PANDA: R01HD086001). The NICHD had no role in study design, data collection, data analysis, data interpretation, or writing of this article. DSM Nutritional Products, LLC Columbia, MD, USA donated the investigational capsules for both the ADORE and PANDA trials. DSM also had no role in the study.

Author statement

SA Crawford: Conceptualization, methodology, data curation, writing-original draft preparation, data curation, formal analysis
DN Christifano: Data curation. Writing – reviewing and editing
EH Kerling: Conceptualization, methodology, supervision, investigation
BJ Gajewski: Software, validation, methodology, formal analysis, resources
CJ Valentine: Conceptualization, methodology
KM Gustafson: Conceptualization
NB Mathis: Visualization, investigation
JT Camargo: Visualization, investigation, formal analysis
HD Gibbs: Supervision
DK Sullivan: Data curation
SA Sands: Investigation
SE Carlson: Supervision, writing – reviewing and editing, visualization, resources

CRediT authorship contribution statement

SA Crawford: Conceptualization, Methodology, Data curation, Writing – original draft, Data curation, Formal analysis. **DN Christifano:** Data curation, Writing – review & editing. **EH Kerling:** Conceptualization, Methodology, Supervision, Investigation. **BJ Gajewski:** Software, Validation, Methodology, Formal analysis, Resources. **CJ Valentine:** Conceptualization, Methodology. **KM Gustafson:** Conceptualization. **NB Mathis:** Visualization, Investigation. **JT Camargo:** Visualization, Investigation, Formal analysis. **HD Gibbs:** Supervision. **DK Sullivan:** Data curation. **SA Sands:** Investigation. **SE Carlson:** Supervision, Writing – review & editing, Visualization, Resources.

Conflict of Interest

SEC has received honorariums for presentations about DHA in infancy and pregnancy. KMG was the PI of R01HD086001. SEC, BJG and CJV were PIs of R01HD083292, CJV was an employee of RB Nutrition, which produces infant formulas and supplements with DHA, however, RB was not involved in the study execution or analysis. She conducted this study through her role as an Adjunct Professor at The University of Cincinnati. The other authors have no competing interests.

Acknowledgments

The study was part of the thesis requirements of SAC for her Master of Science Degree in the Department of Dietetics and Nutrition at the University of Kansas Medical Center. BJG, CJV, KMG and SEC were the principal investigators of the two NICHD funded randomized clinical trials. SAS conducted all RBC-DHA analyses, DNC, EHK, NBM and JTC were responsible for the integrity of data collection in the two trials. HDG, DKS and SEC advised the Master of Science project. CNK developed the DHA-FFQ. SAC and SEC wrote the original draft of the manuscript. All authors reviewed and approved the final version of the manuscript. We thank the pregnant women who participated in the trials. Support for this research came from The National Institutes of Health Child Health and Human Development (NICHD) (ADORE: R01HD083292, PANDA: R01HD086001). DSM Nutritional Products, LLC Columbia, MD, USA donated the investigational capsules for both trials.

References

[1] S.E. Carlson, J. Colombo, B.J. Gajewski, et al., DHA supplementation and pregnancy outcomes, Am. J. Clin. Nutr. 97 (2013) 808–815, https://doi.org/10.3945/ajcn.112.050021.
[2] M.A. Harris, M.S. Reece, J.A. McGregor, et al., The effect of Omega-3 Docosahexaenoic acid supplementation on gestational length: randomized trial of supplementation compared to nutrition education for increasing n-3 intake from foods, BioMed. Res. Int. 2015 (2015), 123078, https://doi.org/10.1155/2015/123078.
[3] S.U. Morton, R. Vyas, B. Gagoski, et al., Maternal dietary intake of Omega-3 fatty acids correlates positively with regional brain volumes in 1-month-old term infants, Cerebral Cortex 30 (2019) 2057–2069, https://doi.org/10.1093/cercor/bhz222.
[4] S.M. Donahue, S.L. Rifas-Shiman, D.R. Gold, et al., Prenatal fatty acid status and child adiposity at age 3 y: results from a US pregnancy cohort, Am. J. Clin. Nutr. 93 (2011) 780–788, https://doi.org/10.3945/ajcn.110.005801.
[5] B.H. Hidaka, J.M. Thodosoff, E.H. Kerling, et al., Intrauterine DHA exposure and child body composition at 5 y: exploratory analysis of a randomized controlled trial of prenatal DHA supplementation, Am. J. Clin. Nutr. 107 (2018) 35–42, https://doi.org/10.1093/ajcn/nqx007.
[6] C. Monthé-Drèze, S. Sen, S. Hauguel-de Mouzon, P.M. Catalano, Effect of Omega-3 supplementation in pregnant women with obesity on newborn body composition, growth and length of gestation: a randomized controlled pilot study, Nutrients 13 (2021) 578, https://doi.org/10.3390/nu13020578.
[7] L. Pereira-da-Silva, C. Cabo, A.C. Moreira, et al., The effect of long-chain polyunsaturated fatty acids intake during pregnancy on adiposity of healthy full-term offspring at birth, J. Perinatol. 35 (2015) 177–180, https://doi.org/10.1038/jp.2014.188.
[8] H. Bisgaard, J. Stokholm, B.L. Chawes, et al., Fish oil–derived fatty acids in pregnancy and wheeze and asthma in offspring, New Eng. J. Med. 375 (2016) 2530–2539, https://doi.org/10.1056/NEJMoa1503734.
[9] S. Hansen, M. Strøm, E. Maslova, et al., Fish oil supplementation during pregnancy and allergic respiratory disease in the adult offspring, J. Allergy Clin. Immunol. 139 (2017) 104–111, https://doi.org/10.1016/j.jaci.2016.02.042. .e104.
[10] R.H.M. de Groot, B.J. Meyer, ISSFAL Official Statement Number 6: the importance of measuring blood omega-3 long chain polyunsaturated fatty acid levels in research, Prostaglandins Leukot. Essent. Fatty Acids 157 (2020), 102029, https://doi.org/10.1016/j.plefa.2019.102029.
[11] L. Arab, Biomarkers of fat and fatty acid intake, J. Nutr. 133 (Suppl 3) (2003) 925s–932s, https://doi.org/10.1093/jn/133.3.925S.
[12] C.G. Walker, L.M. Browning, A.P. Mander, et al., Age and sex differences in the incorporation of EPA and DHA into plasma fractions, cells and adipose tissue in humans, Br. J. Nutr. 111 (2014) 679–689, https://doi.org/10.1017/s0007114513002985.
[13] M.D. Al, A.C. van Houwelingen, G. Hornstra, Relation between birth order and the maternal and neonatal docosahexaenoic acid status, Eur. J. Clin. Nutr. 51 (1997) 548–553, https://doi.org/10.1038/sj.ejcn.1600444.
[14] National Cancer Institute, Register of Validated Short Dietary Assessment Instruments (2020) https://epi.grants.cancer.gov/diet/shortreg/(accessed 30 March 2021).
[15] M.W. Markhus, I.E. Graff, L. Dahl, et al., Establishment of a seafood index to assess the seafood consumption in pregnant women, Food Nutr. Res. 57 (2013) 19272, https://doi.org/10.3402/fnr.v57i0.19272.
[16] G. Parker, G. McClure, B.D. Hegarty, I.G. Smith, The validity of a food frequency questionnaire as a measure of PUFA status in pregnancy, BMC Pregnancy Childbirth 15 (2015) 60, https://doi.org/10.1186/s12884-015-0494-3.
[17] M. Kobayashi, S.C. Jwa, K. Ogawa, N. Morisaki, T. Fujiwara, Validity of a food frequency questionnaire to estimate long-chain polyunsaturated fatty acid intake among Japanese women in early and late pregnancy, J. Epidemiol. 27 (2017) 30–35, https://doi.org/10.1016/j.je.2016.07.001.
[18] J. Lepsch, J.S. Vaz, J.D. Moreira, et al., Food frequency questionnaire as an indicator of the serum composition of essential n-3 and n-6 polyunsaturated fatty acids in early pregnancy, according to body mass index, J. Hum. Nutr. Diet. 28 (2015) 85–94, https://doi.org/10.1111/jhn.12225.
[19] M.T.B. Madsen, A.A. Bjerregaard, J.D. Furtado, et al., Comparisons of estimated intakes and plasma concentrations of selected fatty acids in pregnancy, Nutrients 11 (2019) 568, https://doi.org/10.3390/nu11030568.
[20] M. Shiraishi, M. Haruna, M. Matsuzaki, R. Murayama, S. Sasaki, The biomarker-based validity of a brief-type diet history questionnaire for estimating eicosapentaenoic acid and docosahexaenoic acid intakes in pregnant Japanese women, Asia Pac. J. Clin. Nutr. 24 (2015) 316–322, https://doi.org/10.6133/apjcn.2015.24.2.10.
[21] W.C. Willett, E. Lenart, Reproducibility and Validity of Food-Frequency Questionnaires, in: W.C. Willett (Ed.), Nutritional Epidemiology, Oxford University Press, New York, 1998, pp. 101–147.
[22] F.E. Thompson, A.F. Subar, Dietary Assessment Methology, Nutrition in the Prevention and Treatment of Disease, Academic Press, 2012, pp. 5–30.
[23] National Institutes of Health, Epidemiology and genomics research program, national cancer institute, Diet History Questionnaire (2010). Version 2.0.
[24] C. Kuratko, Food-frequency questionnaire for assessing long-chain omega-3 fatty-acid intake: *re*: assessing long-chain omega-3 polyunsaturated fatty acids: a tailored food-frequency questionnaire is better, Nutrition 29 (2013) 807–808, https://doi.org/10.1016/j.nut.2012.10.013.
[25] S.E. Carlson, B.J. Gajewski, C.J. Valentine, et al., Assessment of DHA on reducing early preterm birth: the ADORE randomized controlled trial protocol, BMC Pregnancy Childbirth 17 (2017) 62, https://doi.org/10.1186/s12884-017-1244-5.
[26] National Cancer Institute, Epidemiology and Genomics Research Program, Diet History Questionnaire II: Frequently Asked Questions. https://epi.grants.cancer.gov/dhq2/help/faqs.html, 2020 (accessed 23 July 2021).
[27] United States Department of Agriculture, Agricultural Research Service, USDA Nutrient Database for Standard Reference. https://www.ars.usda.gov/ARSUserFiles/80400535/DATA/sr14/sr14_doc.pdf, 2002 (accessed 09 April 2021).
[28] K. Yurko-Mauro, D. McCarthy, D. Rom, et al., Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline, Alzheimers Dement 6 (2010) 456–464, https://doi.org/10.1016/j.jalz.2010.01.013.
[29] A.S. Ryan, E.B. Nelson, Assessing the effect of docosahexaenoic acid on cognitive functions in healthy, preschool children: a randomized, placebo-controlled, double-blind study, Clin. Pediatr. (Phila) 47 (2008) 355–362, https://doi.org/10.1177/0009922807311730.
[30] A.F. Subar, F.E. Thompson, V. Kipnis, et al., Comparative validation of the block, Willett, and national cancer institute food frequency questionnaires: the eating at America's table study, Am. J. Epidemiol. 154 (2001) 1089–1099, https://doi.org/10.1093/aje/154.12.1089.
[31] F.E. Thompson, A.F. Subar, C.C. Brown, et al., Cognitive research enhances accuracy of food frequency questionnaire reports: results of an experimental validation study, J. Am. Diet. Assoc. 102 (2002) 212–225, https://doi.org/10.1016/s0002-8223(02)90050-7.
[32] National Cancer Institute, Epidemiology and Genomics Research Program, Background On Diet History Questionnaire II (DHQ-II) For U.S. & Canada. https://epi.grants.cancer.gov/dhq2/about/, 2020 (accessed 31 March 2021).
[33] National Cancer Institute, Epidemiology and genomics research program DHQ-II nutrient database. https://epi.grants.cancer.gov/dhq2/about/citations.html.
[34] National Cancer Institute, Epidemiology and Genomics Research Program, Diet*Calc Analysis Program, Version 1.5.0, October 2012.
[35] National Cancer Institute, Epidemiology and Genomics Research Program, Development of the DHQ II and C-DHQ II Nutrient & Food Group Database. https://epi.grants.cancer.gov/dhq2/database/, 2020 (accessed 31 March 2021).
[36] National Cancer Institute, Epidemiology and Genomics Research Program, Diet History Questionnaire II (DHQ II): Diet*Calc Software. https://epi.grants.cancer.gov/dhq2/dietcalc/, 2020 (accessed 31 March 2021).
[37] P. Schober, C. Boer, L.A. Schwarte, Correlation coefficients: appropriate use and interpretation, Anesth. Analg. 126 (2018) 1763–1768, https://doi.org/10.1213/ane.0000000000002864.
[38] M.M. Mukaka, Statistics corner: a guide to appropriate use of correlation coefficient in medical research, Malawi Med. J. 24 (2012) 69–71.
[39] N.A. Wilson, E. Mantzioris, P.F. Middleton, B.S. Muhlhausler, Influence of sociodemographic, lifestyle and genetic characteristics on maternal DHA and other polyunsaturated fatty acid status in pregnancy: a systematic review, Prostaglandins Leukot. Essent. Fatty Acids 152 (2020), 102037, https://doi.org/10.1016/j.plefa.2019.102037.
[40] N.A. Wilson, E. Mantzioris, P.F. Middleton, B.S. Muhlhausler, Influence of clinical characteristics on maternal DHA and other polyunsaturated fatty acid status in

pregnancy: a systematic review, Prostaglandins Leukot. Essent. Fatty Acids 154 (2020), 102063, https://doi.org/10.1016/j.plefa.2020.102063.
[41] A. Ortiz-Andrellucchi, P. Henríquez-Sánchez, A. Sánchez-Villegas, et al., Dietary assessment methods for micronutrient intake in infants, children and adolescents: a systematic review, Br. J. Nutr. 102 (Suppl 1) (2009) S87–117, https://doi.org/10.1017/s0007114509993163.
[42] B.L. Sullivan, P.G. Williams, B.J. Meyer, Biomarker validation of a long-chain omega-3 polyunsaturated fatty acid food frequency questionnaire, Lipids 41 (2006) 845–850, https://doi.org/10.1007/s11745-006-5039-0.
[43] M. Lucas, G. Asselin, C. Mérette, M.J. Poulin, S. Dodin, Validation of an FFQ for evaluation of EPA and DHA intake, Public Health Nutr 12 (2009) 1783–1790, https://doi.org/10.1017/s1368980008004333.
[44] I. Herter-Aeberli, C. Graf, A. Vollenweider, et al., Validation of a food frequency questionnaire to assess intake of n-3 polyunsaturated fatty acids in Switzerland, Nutrients 11 (2019) 1863, https://doi.org/10.3390/nu11081863.
[45] M.E. Sublette, C.J. Segal-Isaacson, T.B. Cooper, et al., Validation of a food frequency questionnaire to assess intake of n-3 polyunsaturated fatty acids in subjects with and without major depressive disorder, J. Am. Diet. Assoc. 111 (2011) 117–123, https://doi.org/10.1016/j.jada.2010.10.007, e111-112.
[46] Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Dietary Data, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Hyattsville, MD, 2006 https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Dietary.
[47] Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Dietary Data, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Hyattsville, MD, 2016 https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Dietary.
[48] B.J. Meyer, M. Swierk, K.G. Russell, Assessing long-chain ω-3 polyunsaturated fatty acids: a tailored food-frequency questionnaire is better, Nutrition 29 (2013) 491–496, https://doi.org/10.1016/j.nut.2012.04.002.
[49] A.C. Zhang, L.E. Downie, Preliminary validation of a food frequency questionnaire to assess long-chain Omega-3 fatty acid intake in eye care practice, Nutrients 11 (2019) 817, https://doi.org/10.3390/nu11040817.
[50] K.B. Michels, Nutritional epidemiology—Past, present, future, Int. J. Epidemiol. 32 (2003) 486–488, https://doi.org/10.1093/ije/dyg216.
[51] L. Serra-Majem, L. Frost Andersen, P. Henríque-Sánchez, et al., Evaluating the quality of dietary intake validation studies, Br. J. Nutr. 102 (2010) S3–S9, https://doi.org/10.1017/S0007114509993114.
[52] U.S.Environmental Protection Agency, Estimated fish consumption rates for the U. S. population and selected subpopulations (NHANES 2003-2010). https://www.epa.gov/sites/default/files/2015-01/documents/fish-consumption-rates-2014.pdf, 2014 (accessed 09 April 2021).
[53] Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Dietary Data, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Hyattsville, MD, 2018, 1999-https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Dietary.
[54] B. Meyer, *Re*: food-frequency questionnaire for assessing long-chain omega-3 fatty-acid intake, Nutrition 29 (2013) 808–809, https://doi.org/10.1016/j.nut.2013.02.013.
[55] United States Department of Agriculture, Agricultural research service, FoodData Central (2019) https://fdc.nal.usda.gov/index.html(accessed 09 April 2021).
[56] M. Thompson, N. Hein, C. Hanson, et al., Omega-3 Fatty Acid Intake by Age, Gender, and Pregnancy Status in the United States: national health and nutrition examination survey 2003¯2014, Nutrients 11 (2019) 177, https://doi.org/10.3390/nu11010177.
[57] M. Massari, C. Novielli, C. Mandò, et al., Multiple micronutrients and docosahexaenoic acid supplementation during pregnancy: a randomized controlled study, Nutrients 12 (2020) 2432, https://doi.org/10.3390/nu12082432.