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Higher omega-3 index and DHA status in pregnant women compared to lactating women – Results from a German nation-wide cross-sectional study ☆

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ABSTRACT

Introduction: During pregnancy and lactation, there is a high need of long-chain (LC) omega-3 fatty acids (n-3 PUFA), especially docosahexaenoic acid (DHA), for fetus and infant. Also, a low LC n-3 PUFA status during pregnancy is associated with postpartum depression. The aim of this cross-sectional study was to analyze the LC n-3 PUFA status in German women during pregnancy and lactation.

Material and methods: As a part of a nationwide cross-sectional study in which the nutrient status of women in different stages of life was determined, 213 pregnant ($\geq$27th week of gestation) and 127 lactating women between 18 and 44 years were evaluated regarding their LC n-3 PUFA status by measuring the omega-3 index (relative eicosapentaenoic acid (EPA) and DHA concentration in erythrocyte fatty acid).

Results: The mean omega-3 index of the total study population was 6.23 $\pm$ 1.48%. Pregnant women showed significant ($p \leq 0.001$) higher omega-3 index values (6.40 $\pm$ 1.31%) and DHA concentrations (5.91 $\pm$ 1.23%) than lactating women (omega-3 index: 5.50 $\pm$ 1.34%; DHA: 4.79 $\pm$ 1.27%). Woman with LC n-3 PUFA supplementation showed higher omega-3 index values (7.73 $\pm$ 1.28%) vs. women without supplementation (6.04 $\pm$ 1.39%, $p \leq 0.001$). Week of pregnancy, month of lactation as well as smoking were negatively associated with the omega-3 index.

Conclusion: Comprehensive data on the long-term LC n-3 PUFA status of German women during pregnancy and lactation are presented. To evaluate an optimal maternal omega-3 index in view of the fetal and infant development further studies are needed.

1. Introduction

Long chain (LC) omega-3 fatty acids (n-3 PUFA), eicosapentaenoic acid (EPA) and notably docosahexaenoic acid (DHA), are important for the cognitive and visual development of fetus and infants [1]. Although the fetus and infant as well as the placenta are able to convert DHA and EPA from precursor α-linoleic acid (ALA) [2–5], the LC n-3 PUFA status of fetus and infant depends primarily on the maternal LC n-3 PUFA supply and has to be ensured by placental [6] or breast milk transfer [7].

During the rapid growth of brain in late pregnancy [8] high amounts of DHA accumulates in the brain [8,9], with the highest incorporation of over 40 mg DHA per day between week 35 and 40 of gestation [10]. Thus, preterm infants ($<$34 week of gestation) have a higher risk for a lower DHA status than in term infants [11,12]. A higher maternal DHA status reduce the risk of early preterm birth ($<$34 week) [13,14] as well as of preterm birth ($<$37 week) [15,16]. DHA supplementation during pregnancy has also been reported to increase gestational length [13,15], birth weight and head circumference [13]. Beyond, a limited evidence points to an association of a higher maternal DHA status during pregnancy with the risk of colds and illness symptom duration during the first months of life [16], childhood asthma [17], allergic disease [18] and childhood systolic blood pressure [19]. A low fish consumption and maternal LC n-3 PUFA status, respectively DHA, is also associated with postpartum depression [20–23].

After birth, high DHA requirements persist due to the continued development of brain, which extends until the end of second year of life [8]. Breastfeeding is associated with a higher DHA status of infants compared to formula without enriched LC PUFA [24].

Thus, the maternal LC n-3 PUFA status, notably DHA, should be adequate during pregnancy and lactation. The LC n-3 PUFA status depends on the maternal LC n-3 PUFA intake. An average intake of

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at least 200 mg DHA /day is recommended [25–27] which can be achieved by the intake of oily fish once or twice a week [26]. In addition, for the endogenous formation from precursor ALA, an average intake of 1.5 g ALA /day is recommended in pregnant and lactating women [25]. However, based on varying conversion rates of ALA to EPA and DHA, it is more sensible to determine the LC n-3 PUFA concentrations in blood in contrast to the n-3 PUFA intake to assess the LC n-3 PUFA status [28].

Only a few studies have investigated the LC n-3 PUFA status in pregnant and/or lactating women [20,29–33]. The majority of these studies analyzed the LC n-3 PUFA status in plasma [30,31,33], which can be at best indicate the *short-term* intake of LC n-3 PUFA [34,35] and is subject to high biological variability [36].

Therefore, the purpose of this study was to ascertain the LC n-3 PUFA status during pregnancy and lactation in a population of German women by using the omega-3 index (percentage of EPA and DHA on total erythrocyte fatty acids) which reflects the *long-term* status of these fatty acids [37,38] and to assess potential determinants of the LC n-3 PUFA status.

2. Materials and methods

2.1. Study design

The study presented was part of the nationwide, cross-sectional, multicenter VitaMinFemin study (Vitamin- and mineral status among German women) which determined the status of selected nutrients of women in different stages of life. The Institute of Food Science and Human Nutrition, Leibniz University Hannover, Germany, was coordinator and trial center. The study was conducted in 125 study sites of Germany from April 2013 (first patient in) to March 2015 (last patient in). Recruitment of study participants took place in cooperation with gynecologists and general practitioners. Recruiting process and study implementation were independently organized and carried out during the daily practice of the physicians involved. Blood samples were taken as a part of a routinely or diagnostic necessary examination. Completed questionnaire was sent to the trial center. On the day of blood sample, the collection tubes were sent to the laboratory.

The study was designed and conducted in accordance with the declaration of Helsinki and the principles of Good Clinical Practice. Study protocol was approved by the ethics commission of the medical chamber of Lower Saxony (26.03.2013) and every involved ethic commission of different study sites. The clinical trial was registered in the German Clinical Trial Register (identification number: DRKS00004789).

2.2. Subjects

The present analysis is based on a sample of 378 women which fulfilled the inclusion criteria (pregnancy in the third trimester ($\geq$ 27th gestational week) or lactation) (Fig. 1). Every subject had to give their written informed consent. General exclusion criteria were: diagnostic blood coagulation disorders, intake of coagulation-inhibiting drugs (such as phenprocoumon), chronic gastrointestinal disorders (e.g. ulcers, Crohn's disease, pancreatic insufficiency), chronic diseases (tumor, diabetes mellitus type 1, etc.), manifest cardiovascular diseases, renal failure, liver diseases, regular intake of laxatives, alcohol-, drugs- and/or medicine dependency, retraction of the consent by the subject, coincident participation in another clinical study, participation in a study in the last 30 days. 39 woman supplemented LC n-3 PUFAs. The intake of dietary supplements was determined by questionnaires.

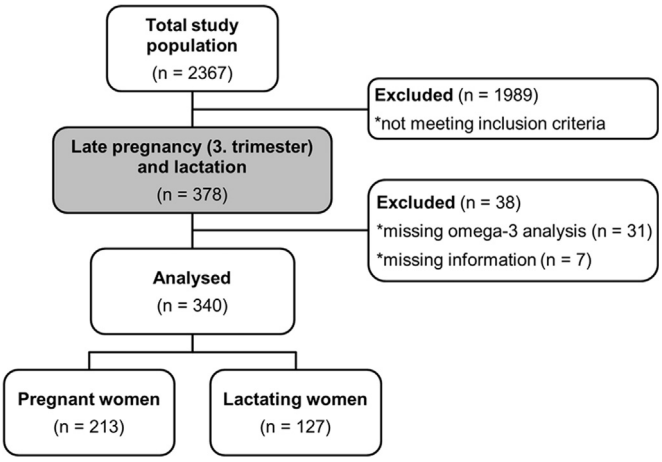

Fig. 1. Recruitment of study subjects.

2.3. Omega-3 index and fatty acid levels in erythrocyte membranes analysis

Fatty acid levels in erythrocyte membranes were analyzed according to the omega-3 index methodology as described previously [37]. The omega-3 index is defined as the relative EPA und DHA concentration in relation to total fatty acids in erythrocyte membranes. Fatty acid methyl esters were generated from erythrocytes by acid transesterification and analyzed by gas chromatography using a GC2010 Gas Chromatograph (Shimadzu, Duisburg, Germany) equipped with a SP2560, 100-m column (Supelco, Bellefonte, PA) using hydrogen as carrier gas. Fatty acids were identified by comparison with a fatty acid standard mixture characteristic for erythrocytes. Results are given as EPA plus DHA expressed as a percentage of total identified fatty acids after response factor correction. The coefficient of variation for EPA plus DHA was 5%. Quality was ensured in accordance to DIN ISO 15189.

2.4. Data analysis and statistics

Fatty acid levels and omega-3 index values were evaluated for the total study population as well as different subgroups (pregnant vs. lactating woman, supplement vs. non-supplement users) separately.

To evaluate region-specific differences in the omega-3 index categorization of region was carried out in accordance with recruiting site (north: Mecklenburg-Western Pomerania, Lower Saxony, North Rhine-Westphalia, Berlin, Brandenburg; south: Saarland, Rhineland-Palatinate, Thuringia, Hessen, Saxony, Bavaria, Baden-Wuerttemberg).

The statistical analysis was conducted by the statistical package for social science (SPSS) version 22 (SPSS, Inc. Chicago, Illnois, USA). Results were shown as mean $\pm$ standard deviation ($\pm$ SD) and range (minimum–maximum), median or frequency and percent. Normal distribution was tested by Kolmogorov-Smirnov Test. Statistical differences between subgroups were analyzed by non-parametric Mann-Whitney-*U* test. Differences between the categorical variables were tested by using Chi-square test. In case of skewed distribution, a multiple linear regression was performed. The model can be regarded as robust, as the forward, backward and stepwise selection showed equal variable combinations. Significance level was $p < 0.05$.