Long-chain polyunsaturated fatty acid status in first-trimester pregnant women

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ABSTRACT

Background: The beneficial effects of long-chain polyunsaturated fatty acid (LCPUFA) on maternal health have been widely investigated in pregnant women. First-trimester supplementation of LCPUFA has been reported to play a role in the inflammatory response, thus reducing a preterm birth and preeclampsia. However, there is a lack of studies investigating the blood concentration of LCPUFA in pregnant women in Indonesia. This study was conducted to evaluate the status of LCPUFA in first-trimester pregnant women in Jakarta, Indonesia.

Methods: A descriptive study was conducted using the secondary data of 197 pregnant women in their first trimester who received antenatal care in Budi Kemuliaan Hospital during February 2012 to April 2015. Nutrient intake data were collected through interviews conducted using a semi-quantitative frequency food questionnaire (SQ-FFQ). Total concentrations of linoleic acid (LA), arachidonic acid (AA), alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) were measured using gas-chromatography/mass spectrometry (GC-MS). Statistical analysis of the data was conducted using SPSS 20.0.

Results: Most subjects had deficient blood concentrations of LA (74.1%), AA (85.3%), ALA (76.6%), and DHA (73.1%). The median total concentrations of LA, AA, ALA, EPA, and DHA were as follows: 76.08%, 14.97%, 2.64%, 6.36%, and 1.18%, respectively. The median EPA+DHA level was 7.98%. A total of 38 women (19.3%) were classified as high-risk subjects based on the omega-3 index. No correlation was observed between total DHA+EPA concentration and birth weight ($r=0.027$, $p=0.709$). However, a significant difference was detected between the concentrations of LA, AA, and ALA and the maternal body mass index ($p<0.05$).

Conclusion: Most subjects had low intake and blood concentrations of LA, AA, ALA, EPA, and DHA in the first trimester of pregnancy.

Keywords: DHA, EPA, LCPUFA, low birth weight

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Long-chain polyunsaturated fatty acid (LCPUFA) is widely known for its vital role in pregnancy outcome. Maternal LCPUFA deficiency has been reported to increase the risks of preeclampsia, preterm birth, and fetal growth restriction.[1–3] Docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and arachidonic acid (AA) have been demonstrated to exert a proangiogenic effect in extravillous trophoblast cell lines. Carvajal demonstrated that DHA reduces oxidative stress, which is the key role in deep placentation disorders.[4] It has also been suggested that DHA is partly responsible for the inhibition of E_2 and F_2 prostaglandins involved in the ripening of the cervix and relaxes uterine smooth muscles through increased production of PGI2 and PGI3 levels.[1]

AA, EPA, and DHA are the major LCPUFAs that are formed from the fatty acid precursors alpha-linolenic acid (ALA) and linoleic acid (LA). Both ALA and LA are essential fatty acids that must be obtained from foods such as vegetable oils and soybean.[5,6] The fetus is capable of converting ALA into DHA and LA into AA; however, sufficient LCPUFA is needed to provide and meet the high requirements. Therefore, fetal LCPUFA supply is highly dependent on the maternal dietary intake of DHA and AA.[5]

Current review recommends 200 mg DHA per day for pregnancy and lactation. DHA intake must be balanced with the intake of AA, since DHA intake might increase the susceptibility to AA deficiency. DHA intake must be accompanied by a sufficient supply of AA with a ratio of 2:1 of AA:DHA.[5,7] The timing of the supplementation should probably start as early as the first trimester in pregnancy, as it has been reported that after 16 weeks of pregnancy, the supplementation failed to demonstrate an effect.[4] Although there are studies on LCPUFA regarding its beneficial effects on maternal and fetal health, there is a lack of research on the status of LCPUFA in pregnant women population. Till date, there are no data regarding the blood concentration of LCPUFA in pregnant women in Indonesia. Therefore, this study was conducted to evaluate the status of LCPUFA in first-trimester pregnant women in Indonesia.

METHODS

Data were obtained from two previous interventional studies conducted in Budi Kemuliaan Hospital, Jakarta, during February 2012 to April 2015, which were approved by the Ethical Committee for Research in Human from the Faculty of Medicine, Universitas Indonesia (No. 480/PT02.FK/ETIK/2012 and No. 71/H2.F1/ETIK/2013). This investigation was a descriptive analytic study of 197 pregnant women in their first trimester who received antenatal care. The inclusion criteria were women of no more than 13 weeks of gestational age. The exclusion criteria were subjects with incomplete data. All the subjects agreed to participate in this study.

The basic characteristics of the subjects, e.g., maternal age, education, occupation, and body mass index (BMI), were examined. The term "highly educated" was defined as a junior high graduate and above. BMI was categorized into low BMI (<18.5 kg/m^2), normal BMI (18.5–22.9 kg/m^2), and high BMI (≥23 kg/m^2) according to the World Health Organization classification of BMI and modified for Asians. BMI examination was performed during the first visit in the first trimester. The data presented were nutrient intake from subjects' recall using a semi-quantitative frequency food questionnaire (SQ-FFQ) for a month and the blood test results of a blood count and nutrient levels. The FFQ data were then converted into food nutrient intake using the Nutrisurvey program with food database from Indonesia.

Samples for the first-trimester blood analysis were obtained between 6 and 13 weeks of gestation. The total concentrations of LA, AA, ALA, EPA, and DHA were measured using gas-chromatography/mass spectrometry (GC-MS). Data were analyzed using SPSS 20 and presented as mean±SD if normally distributed and as median (minimum–maximum) if not normally distributed. The Spearman or the Pearson test was performed to determine the correlation between variables.

RESULTS

Characteristics of the subjects

A total of 197 pregnant women in their first trimester were included in this study. The characteristics of the subjects are shown in Table 1. The median age was 29 (19–43) years, which was within the range of optimal reproductive age. Most subjects were highly educated (94.4%), working (56.3%), and had

Table 1. Characteristics of the subjects (n=197)

Variable	Frequency (%)
Maternal age (years)	29 (19–43)*
Education	
Highly educated	186 (94.4)
Low educated	11 (5.6)
Occupation	
Working	111 (56.3)
Housewife	86 (43.7)
BMI	
Low	
Underweight (<18.5)	19 (9.6)
Normal	
Normal (18.5–22.9)	81 (41.1)
High	
Overweight (23–24.9)	28 (14.2)
Pre-obese (25–29.9)	52 (26.4)
Obese (≥30)	13 (6.6)
Gestational age at delivery	
Term (≥37 weeks)	192 (97.5)
Preterm (<37 weeks)	5 (2.5)
Hypertension in pregnancy	
Yes	7 (3.6)
No	190 (96.4)
Birth weight (g)	3200 (800–4250)*
<2,500	9 (4.6)
≥2,500	188 (95.4)

*Median (minimum–maximum)

BMI above the normal range (47.2%). During the observation, there were five subjects (2.5%) undergoing preterm labor and seven subjects (3.6%) with hypertension in pregnancy, and nine babies (4.6%) had low birth weight.

First-trimester PUFA status and intake

Details regarding the intake and status of PUFA of subjects in the first trimester are shown in Table 2. Most of the subjects had low blood concentrations of LA (74.1%), AA (85.3%), ALA (76.6), and DHA (73.1%). The median (range) values of LA [1360.55 (20.13–8986.67)], AA [300 (21.97–874.91)], ALA [24.87 (1.15–544.9)], and DHA [17.98 (1.19–163.49)] were below the normal range.

The total concentration of fatty acids is expressed as the % weight of total fatty acids. The total concentrations of omega-6 fatty acids were 76.08 (range: 2.8–97.81) for LA and 14.97 (range: 1–88.43) for AA. The highest concentration was found for the omega-3 fatty acid EPA [6.36 (range: 0.08–64.46)]. Based on the omega-3 index, i.e., the sum of EPA and DHA, a total of 38 subjects (19.3%) were found to be at high risk. The median omega-6 to omega-3 ratio was 9.33 (range: 0.51–348.84).

Regarding the daily intake of PUFA, there was a correlation between PUFA intake and total AA (r=0.199, p=0.005) and total LA (r=0.158, p=0.027) concentrations. However, no correlation existed between total DHA+EPA concentration and birth weight (r=0.027, p=0.709).

A nonparametric test was conducted to determine the significant differences between maternal BMI and LCPUFA concentrations. We detected significant differences in ALA concentrations between subjects with BMI <18.5 and those with BMI >23 (p=0.005) and between subjects with normal BMI and those with high BMI of >23 (p=0.022). The ALA concentrations were higher in subjects with BMI >23 than those in subjects with lower BMI.

DISCUSSION

The blood concentrations of DHA were found to be lower in this study than in several studies.[8–9] Dwarkanath et al[10] also reported similar DHA levels in the first trimester in pregnant women in India, with a median value of 1.97 (range: 1.57–2.65) μM. Based on the first systematic review on the global status of PUFA, our findings fell into the higher category of EPA+DHA. Stark et al categorized EPA+DHA levels into very low (<4%), low (>4%–6%), moderate (>6%–8%), and high (>8%). Although the PUFA intake of Southeast Asian nations fell into the very low category, most of the subjects in this study had an omega-3 index of >4.[11]

The median PUFA intake [4.15 (range: 0.10–15.00) g/day] was lower than the recommended daily allowance (RDA) of the Decree of Ministry of Health of Republic Indonesia No. 75 year 2013, which is 15.4 g/day.[12] This study also demonstrated that most of the subjects had low blood concentrations of all omega-6 and omega-3 fatty acids, except EPA. This result is

Table 2. First-trimester PUFA status and intake

Variable	Median (min–max)	n (%)
Blood concentration (µMol/L)		
Omega-6		
LA	1360.55 (20.13–8986.67)	
Low (<2270)		146 (74.1)
Normal (2270–3850)		42 (21.3)
High (>3850)		9 (4.6)
AA	300 (21.97–874.91)	
Low (<520)		168 (85.3)
Normal (520–1490)		29 (14.7)
Omega-3		
ALA	24.87 (1.15–544.9)	
Low (<50)		151 (76.6)
Normal (50–130)		37 (18.8)
High (>130)		9 (4.6)
EPA	20.35 (0.06–218.11)	
Low (<14)		78 (39.6)
Normal (14–100)		89 (45.2)
High (>100)		30 (15.2)
DHA	17.98 (1.19–163.49)	
Low (<30)		144 (73.1)
Normal (30–250)		53 (26.9)
Total concentration (%)		
Omega-6		
LA	76.08 (2.8–97.81)	
AA	14.97 (1–88.43)	
Omega-3		
ALA	2.64 (0.05–25.77)	
EPA	6.36 (0.08–64.46)	
DHA	1.18 (0.12–23.21)	
Omega-3 index (EPA+DHA)		
High risk (<4)		38 (19.3)
Intermediate risk (4–8)		61 (28.0)
Low risk (>8), n (%)		98 (49.7)
Omega-6 to omega-3 ratio, median (min–max)	9.33 (0.51–348.8)	
Low (<3.4)		3 (1.5)
Normal (3.4–10.7)		97 (49.2)
High (>10.7)		97 (49.2)
Daily Maternal Intake		
PUFA (g)	4.00 (0.10–15.00)	

LA=linoleic acid; AA=arachidonic acid; ALA=alpha-linolenic acid; EPA=eicosapentaenoic acid; DHA=docosahexaenoic acid; PUFA=polyunsaturated fatty acid

consistent with Angkasa et al who observed that pregnant women in Jakarta had a low total intake of omega-3 fatty acids, which was associated with lower newborn weights.[13] As Jakarta is an urban city comprising multicultural citizens with a wide gap of educational and financial status, the source of fat intake varies. However, Hatma et al[14] investigating the intake of fatty acids among

diverse ethnic groups in Indonesia found that the ethnic groups Minangkabau, Sundanese, Javanese, and Buginese had a lower PUFA intake than the Indonesian RDA (4.7, 8.8, 6.1, and 3.7 g/day, respectively), with the fatty acid ratio, presumed as the ratio of polyunsaturated fatty acids to saturated fatty acids (SFAs), being approximately or <0.2, which is considered as an atherogenic diet. Indeed, a systematic review on the intake of fatty acids in 40 countries found that the mean Indonesian PUFA intake is 3.5 g/day, ranking the second lowest in the list. In contrast, a low PUFA intake was accompanied by a high intake of SFAs. This might be caused due to the high consumption of coconut and palm oils that contain a high proportion of SFAs.[15]

The median omega-6 to omega-3 ratio was 9.33, which falls into the normal range, i.e., 3.4–10.7.Over the years, the dietary shift toward a "western diet" containing excessive levels of omega-6 PUFAs but very low levels of omega-3 PUFAs has resulted in a drastic change in the ratio to about 20–30:1. The metabolism of omega-6 PUFA is considered to be proinflammatory, whereas the metabolism of omega-3 PUFA produces anti-inflammatory lipid mediators. The metabolic products from AA, the simplest form of omega-6 PUFA, are prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids, and lipoxins, which contribute to the formation of thrombus and atheroma, rendering the physiological state to proinflammatory, prothrombotic, and proaggregatory. Omega-3 PUFA inhibits the production of nuclear factor-kappa beta (NFκB), which is a transcription factor for several proinflammatory cytokines such as TNF-α and IL. It also reduces the gene expression of IL-6 and IL-1β. Foods considered to be high in omega-6 PUFA include refined oil that is frequently used in processed food and cakes, peanuts, almonds, cashews, pumpkin seeds, and coconut oil. Omega-3 PUFA can be obtained primarily from fatty fish such as mackerel, salmon, sardines, and anchovies, as well as flaxseeds, chia seeds, and soybeans.[16,17]

We acknowledge certain limitations in this study. The study population from Budi Kemuliaan Hospital primarily included patients from Central Jakarta, and therefore, it did not represent the population of Jakarta. In addition, we did not evaluate the financial status of the subjects, which has a great influence on the nutrient intake pattern. The FFQ method used in this study depended on the subjects' memory, thus rendering it less objective despite the utilization of a food model to reduce bias.

In conclusion, most pregnant women in Jakarta had low intake and blood concentrations of LCPUFA, except for the blood concentration of EPA. Hence, understanding the importance of PUFA to support fetal growth and development as well as to prevent poor pregnancy outcome and encouraging increased intake of PUFA through meals or supplementation are imperative, in addition to reducing the omega-6 to omega-3 ratio and increasing the P/S ratio.

Conflict of interest

The authors affirm no conflict of interest in this study.

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