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Differential levels of long chain polyunsaturated fatty acids in women with preeclampsia delivering male and female babies

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ABSTRACT

Maternal long chain polyunsaturated fatty acids (LCPUFA) play a key role in fetal growth and development. This study for the first time examines the maternal and cord LCPUFA levels in preeclamptic mothers delivering male and female infants. In this study 122 normotensive control pregnant women (gestation $\geq$ 37 weeks) and 90 women with preeclampsia were recruited. Results indicate lower maternal plasma docosahexaenoic acid (DHA) levels ($p < 0.05$) in women with preeclampsia delivering male babies as compared to normotensive control women delivering male babies. Similarly, cord nervonic acid levels were lower ($p < 0.01$) in women with preeclampsia delivering male babies as compared to normotensive control group. However, cord nervonic acid levels were comparable in women with preeclampsia and normotensive control women delivering female babies. This data suggests that male babies born to mothers with preeclampsia may be at an increased risk of developing neurodevelopmental disorders as compared to female babies. Future studies need to follow up both male and female children born to mothers with preeclampsia since altered levels of LCPUFA at birth may have differential implications for the growth and development.

1. Introduction

Preeclampsia a leading cause of maternal and fetal mortality and morbidity worldwide is widely believed to be due to improper placentation [1]. Our earlier cross sectional studies have demonstrated the association of altered maternal micronutrition especially long chain polyunsaturated fatty acids (LCPUFA) status in women with preeclampsia [2,3]. The two types of LCPUFA i.e. omega-3 and omega-6 fatty acids which are components of cell membranes and are important for fetal growth and development [4,5]. Linoleic acid (LA) an omega-6 fatty acids and alpha-linolenic acid (ALA), an omega-3 fatty acid are converted to arachidonic acid (AA) and docosahexaenoic acid (DHA) by the series of elongation and desaturation using elongases and desaturases enzymes [6,7].

In humans AA and DHA play a vital role in brain development [8,9]. In childhood, omega-3 fatty acids especially DHA is reported to influence cognitive development [10,11]. Nervonic acid an omega-9 fatty acid is a component of membrane sphingolipids and phosphatidylethanolamines [12] and recent studies suggest its involvement in learning and memory [13]. These fatty acids are of significance since children born to mothers with preeclampsia are reported to be at an increased risk of developing neurodevelopmental disorders in later life [14–16]. Reports indicate that many early onset neurodevelopmental disorders are male-biased, that is they occur significantly more often in males than females [17].

Recent studies indicate that the gender distribution needs to be taken into account while assessing data on fatty acid composition [18]. Females are reported to have a higher DHA status than males [19]. Studies also suggest that sex hormones may influence the enzymatic synthesis of LCPUFA, which may lead to sex-specific differences in LCPUFA status [20]. Reports indicate that there is an association between plasma and tissue fatty acid composition and circulating sex hormone concentrations, estrogen stimulates, whereas testosterone inhibits, the conversion of essential fatty acids into their longer-chain metabolites [21].

Preeclampsia originates in the placenta, starting with inadequate cytotrophoblast invasion and ending with widespread maternal endothelial dysfunction [22]. It has been suggested that hypoxia, placental oxidative stress, excessive or atypical maternal immune response to trophoblasts, exaggerated inflammation may play a role

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in poor placentation in preeclampsia [23]. Sex specific alterations in placental genes involved with growth and inflammation are reported in cases of maternal hypoxia suggesting that aberrations in placental functions can occur in a sex specific manner [24]. Further, recent reports also indicate that there exists a sex specific difference in feto-placental perfusion indices [25].

However it is unclear whether the sex of the fetus is associated with maternal and cord levels of LCPUFA levels in preeclampsia and normotensive control. The present study was carried out to test the hypothesis that "LCPUFA levels in mothers with preeclampsia delivering male and female babies and their cord samples may be different".

2. Materials and methods

2.1. Study subjects

This study was conducted at the Dept of Obstetrics and Gynecology, Bharati Hospital, Pune during the year 2011–2013. The research protocol was approved by the Institutional Ethical Committee. A written consent was taken from women participating in the study. Healthy pregnant women with no medical or obstetrical complications and delivered at term (total gestation ≥ 37 weeks) were recruited for the normotensive control (normotensive control, $n=122$) group study. Women with preeclampsia (preeclampsia; $n=90$) were also recruited. Further, these groups were classified as women delivering male (normotensive control = 69, preeclampsia = 54) and female (normotensive control = 53, preeclampsia = 36) babies.

Preeclampsia was defined by systolic and diastolic blood pressures (BP) greater than 140/90 mmHg respectively, with the presence of proteinuria (> 1+ or 300 mg) on a dipstick test and recorded at two time points > 6 h apart. This diagnosis of preeclampsia and the inclusion exclusion criteria have been reported by us earlier [2,3,26,27]. Birth outcome parameters like baby weight, length, head and chest circumference were recorded within 1 h after birth.

The statistical power was calculated based on our earlier study in preeclampsia [28] where we have reported significant group differences in homocysteine levels from 49 preeclamptic and 57 normotensive women ($p<0.01$).

2.2. Sample collection and processing

10 ml of maternal venous blood was collected into the ethylenediamine tetra-acetic acid (EDTA) vials just before delivery. All blood samples were immediately layered on histopaque (a density gradient obtained from Sigma-Aldrich) and centrifuged at 2000 rpm for 30 min to separate the plasma and erythrocytes. The erythrocytes aliquots were stored at −80 °C until further analysis.

2.3. Plasma fatty acid estimation

The procedure for fatty acid analysis used in this study has been reported by us earlier in separate studies [3,26,28,29]. Briefly, transesterification of plasma and erythrocyte fraction was carried out using hydrochloric acid-methanol.

These were separated using a Perkin-Elmer gas chromatograph (SP 2330, 30 m capillary Supelco column). Helium was used as the carrier gas at a flow rate of 1 ml/min. Oven temperature was held at 150 °C for 10 min, programmed to rise from 150 °C to 220 °C at 10 °C/min and held at 220 °C for 10 min. The detector temperature was 275 °C and the injector temperature was 240 °C. Retention times and peak areas were automatically computed. Peaks were identified by comparison with standard fatty acid methyl esters (Sigma). Fatty acids were expressed as g/100 g fatty acid i.e. percentage of total fatty acids.

Omega-3 fatty acids included ALA, eicosapentaenoic acid (EPA) and DHA while the omega-6 fatty acids included LA, γ-linolenic acid (GLA), dihomo-γ-linolenic acid (DGLA), AA and docosapentaenoic acid (DPA). Saturated fatty acids (SFA) included myristic acid, palmitic acid and stearic acid while the monounsaturated fatty acids (MUFA) included myristoleic acid, palmitoleic acid, oleic acid and nervonic acid.

2.4. Statistical analysis

Values are expressed as mean ± SD. The data were analyzed using SPSS/PC + statistical package (Version 20, Chicago IL). Data was checked for normal distribution by testing for skewness and kurtosis. Skewed variables were transformed to normality using the following transformations: log to the base10 (DHA, AA, nervonic acid, ALA, LA). Mean values of the estimates of various parameters for preeclampsia were compared with those of normotensive control group at conventional levels of significance ($p<0.05$, $p<0.01$) using one way ANOVA method. The interaction between the variables (DHA, AA, nervonic acid, ALA, LA, omega-3 and omega-6) with gender in each group was analyzed by two way ANOVA method.

3. Results

3.1. Maternal and neonatal characteristics

The systolic and diastolic blood pressures were higher in women with preeclampsia as compared to the normotensive control women ($p<0.01$). Baby weight, length, chest circumference and head circumference were lower ($p<0.01$) in the preeclampsia group as compared to normotensive control group (Table 1).

3.2. Maternal plasma fatty acid levels in different groups

Maternal plasma MUFA levels were higher in women with preeclampsia ($p<0.01$) as compared with women in normotensive control group. However, no change was seen in case of SFA in the preeclampsia group. Further, ALA ($p<0.05$), DHA ($p<0.01$) and total omega-3 fatty acids ($p<0.01$) was lower in the preeclampsia group as compared with normotensive control women. There was no difference in case of maternal plasma nervonic acid (Table 2).

3.3. Maternal plasma fatty acids in women delivering male and female babies

MUFA levels were higher ($p<0.01$) in women with preeclampsia delivering male babies as compared with the women delivering male babies in normotensive control group. There was no change in case of SFA levels in any of these groups. DHA levels were lower only in women with preeclampsia delivering male babies as compared to those from normotensive control group ($p<0.05$) while omega-3 fatty acid levels were lower in women with preeclampsia delivering male ($p<0.05$) as compared to normotensive control women delivering male babies. Omega-3 fatty acid levels were also lower in female babies ($p<0.05$) when compared to respective women from normotensive control group. There was no change in case of omega-6 fatty acids and nervonic acid levels (Table 3).

Table 1
Maternal and neonatal characteristics in different groups.

Maternal characteristics	Normotensive control $n=122$ (Mean ± SD)	Preeclampsia $n=90$ (Mean ± SD)
Age (yr)	24.34 ± 4.06	23.57 ± 3.58
BMI (kg/m^2)	21.65 ± 4.10	25.25 ± 4.62
Gestation (wks)	39.10 ± 1.05	37.30 ± 2.56**
Sys BP (mmHg)	120.70 ± 10.24	149.35 ± 16.80**
Dias BP (mmHg)	78.12 ± 7.18	98.13 ± 10.57**
Income (INR)	7814 ± 5012	8245 ± 5126
Parity		
Nulliparous n (%)	38.5	63.3
Multiparous n (%)	61.5	36.7
Mode of delivery		
Normal (%)	73.8	64.0
Cesarean (%)	23.8	36.1
Education (grade) (%)		
Illiterate	5.7	7.8
Primary	6.6	6.7
Secondary	45.1	44.4
Higher secondary	20.5	21.1
Graduation	20.5	18.9
Post graduation	1.6	1.1
Neonatal characteristics		
Baby weight (kg)	2.89 ± 0.28	2.39 ± 0.69**
Baby length (cm)	47.94 ± 2.51	45.52 ± 3.32**
Baby head circumference (cm)	33.56 ± 1.35	32.11 ± 2.54**
Baby chest circumference (cm)	32.15 ± 1.49	29.45 ± 3.54**

Values are expressed as Mean ± SD. Significance:
* $p < 0.05$.
** $p < 0.01$ when compared with normotensive control. BMI: body mass index.

Table 2
Maternal plasma fatty acids in different groups.

Fatty acid (g/100 g fatty acids)	Normotensive control ($n=122$)	Preeclampsia ($n=90$)
Myristic acid	0.85 ± 0.32	0.96 ± 0.30
Myristoleic acid	0.04 ± 0.06	0.06 ± 0.07
Palmitic acid	27.01 ± 2.97	28.22 ± 3.23
Palmitoleic acid	1.66 ± 0.90	2.13 ± 1.06
Stearic acid	6.17 ± 2.57	6.21 ± 2.04
Oleic acid	15.82 ± 2.50	17.60 ± 2.63
Linoleic acid	31.65 ± 8.00	30.31 ± 6.89
γ-Linolenic acid	0.21 ± 0.09	0.26 ± 0.14
α-Linolenic acid	0.39 ± 0.25	0.32 ± 0. 20*
Dihomo-γ-linolenic acid	1.48 ± 0.55	1.49 ± 0.45
Arachidonic acid	6.66 ± 3.11	5.92 ± 2.08
Eicosapentaenoic acid	0.35 ± 0.32	0.26 ± 0.25
Nervonic acid	0.61 ± 0.33	0.54 ± 0.24
Docosapentaenoic acid	0.30 ± 0.20	0.18 ± 0.11**
Docohexaenoic acid	1.20 ± 0.49	1.07 ± 0.34**
Saturated fatty acids	34.04 ± 4.44	35.39 ± 4.05
Monounsaturated fatty acids	18.16 ± 2.61	20.34 ± 3.04**
Total n-3 fatty acids	1.95 ± 0.66	1.67 ± 0.51 **
Total n-6 fatty acids	40.32 ± 5.79	38.17 ± 5.75
n-6/n-3 ratio	23.25 ± 9.01	25.65 ± 10.73*

Values are expressed as Mean ± SD. Significance:
* $p < 0.05$.
** $p < 0.01$ when compared with normotensive control.

3.4. Cord plasma fatty acid levels in different groups

MUFA levels were higher ($p < 0.01$) in the preeclampsia group as compared with normotensive control women and no change was observed in case of SFA levels. Cord plasma ALA ($p < 0.01$), DHA ($p < 0.05$) and total omega-3 fatty acids ($p < 0.05$) was lower in the preeclampsia group as compared with normotensive control women. In case of total omega-6 fatty acids only AA was lower but not statistically significant in women with preeclampsia group as compared with normotensive control group. Nervonic acid was lower ($p < 0.01$) in the women with preeclampsia as compared with normotensive control (Table 4).

3.5. Cord plasma fatty acids in women delivering male and female babies

MUFA levels were higher ($p < 0.05$) in women with preeclampsia delivering male and female babies as compared to those women in normotensive control group. There was no change in case of SFA levels in any of these groups. ALA ($p=0.056$) and total omega-3 fatty acid ($p=0.054$) levels were marginally lower in the preeclampsia group. ALA levels were lower ($p < 0.05$) in women with preeclampsia delivering male babies as compared to those women in normotensive control group. AA were lower ($p < 0.05$) in women with preeclampsia delivering male babies as compared to those women in normotensive control group. The nervonic acid levels were lower ($p < 0.01$) in women with preeclampsia delivering male babies as compared to normotensive control group (Table 5).

4. Discussion

This study for the first time reveals very interesting findings in women with preeclampsia as compared to those women in normotensive control group 1) Lower maternal plasma ALA, DHA and total omega-3 fatty acids 2) Lower cord plasma ALA, DHA, nervonic acid and total omega-3 fatty acid levels 3) Further, lower maternal plasma DHA levels in women with preeclampsia delivering male babies as compared normotensive control women delivering male babies 4) Lower cord plasma AA and nervonic acid levels in women with preeclampsia delivering male babies as compared to normotensive control women delivering male babies while levels were comparable in women delivering female babies.

This study for the first time reports the maternal and cord LCPUFA levels based on the baby gender in preeclampsia. Higher amount of DHA concentrations in females as compared to the males has been reported in healthy adult humans [30,31]. Similarly, animal studies report higher AA and DHA plasma and liver phospholipid levels in female than male rats [32,33].

Sex hormones are suggested to influence the activity of desaturase enzymes which are involved in the synthesis of LCPUFA. Both animal studies [33] and human stable-isotope studies, indicate that females have a higher capacity than males to synthesize DHA from ALA [34,35]. Both estradiol and testosterone hormones are reported to alter the expression of desaturase ($\Delta9/\Delta5/\Delta6$-desaturase) and elongase enzymes in the liver [21].

In the current study DHA and omega-3 fatty acids levels were lower although there was no change in AA levels in women with preeclampsia delivering male babies. The altered levels of PUFA in women delivering male babies in our study could be due to the steroid hormones which modify desaturase by increasing $\Delta9$ expression and by decreasing $\Delta5$ and $\Delta6$ desaturase enzymes [36].

In contrast, in the current study, the cord levels of DHA were lower in women with preeclampsia delivering female babies as compared to those women in normotensive control group. The mammalian placenta provides a highly estrogenic environment for both female and male fetuses [37], however it has been also reported that estrogen levels in women with preeclampsia are lower than normotensive women [38]. The lower cord DHA levels in females observed in this study may possibly be due to the lower

Table 3
Maternal plasma fatty acids in women delivering male and female babies.

Fatty acid (g/100 g fatty acids)	Normotensive control (n=122)		Preeclampsia (n=90)	
	Male (n=69)	Female (n=53)	Male (n=54)	Female (n=36)
Myristic acid	0.88 ± 0.33	0.81 ± 0.31	9.08 ± 0.28	0.92 ± 0.33
Myristoleic acid	0.04 ± 0.07	0.04 ± 0.05	0.06 ± 0.09*	0.04 ± 0.03
Palmitic acid	26.99 ± 3.00	27.04 ± 2.96	28.06 ± 3.03	28.46 ± 3.53
Palmitoleic acid	1.69 ± 0.83	1.63 ± 1.00	2.25 ± 1.11*	1.96 ± 0.95
Stearic acid	6.27 ± 3.04	6.04 ± 1.78	6.36 ± 2.43	5.97 ± 1.26
Oleic acid	15.70 ± 2.62	15.98 ± 2.35	17.79 ± 2.69	17.32 ± 2.56
Linoleic acid	31.40 ± 8.49	31.97 ± 7.39	29.38 ± 7.26	31.80 ± 6.11
γ-Linolenic acid	0.21 ± 0.09	0.22 ± 0.09	0.26 ± 0.13	0.25 ± 0.15
α-Linolenic acid	0.40 ± 0.27	0.38 ± 0. 22	0.33 ± 0.19	0.31 ± 0.20
Dihomo-γ-linolenic acid	1.49 ± 0.53	1.46 ± 0.59	1.50 ± 0.43	1.47 ± 0.49
Arachidonic acid	6.65 ± 3.16	6.67 ± 3.08	6.16 ± 2.29	5.54 ± 1.67*
Eicosapentaenoic acid	0.34 ± 0.30	0.36 ± 0.34	0.25 ± 0.24	0.29 ± 0.27
Nervonic acid	0.65 ± 0.39	0.57 ± 0.23	0.54 ± 0.28	0.54 ± 0.18
Docosapentaenoic acid	0.30 ± 0.22	0.31 ± 0.16	0.17 ± 0.12**	0.19 ± 0.102;@@
Docohexaenoic acid	1.18 ± 0.51	1.22 ± 0.46	1.09 ± 0.34*	1.03 ± 0.33
Saturated fatty acids	34.15 ± 4.92	33.90 ± 3.77	35.41 ± 4.06	35.37 ± 4.06
Monounsaturated fatty acids	18.10 ± 2.68	18.23 ± 2.54	20.66 ± 3.29**	19.86 ± 2.62
Total n-3 fatty acids	1.94 ± 0.65	1.98 ± 0.67	1.68 ± 0.50*	1.65 ± 0.541;@
Total n-6 fatty acids	40.07 ± 6.1	40.65 ± 5.41	37.44 ± 5.89	39.28 ± 5.43
n-6/n-3 ratio	23.13 ± 8.43	23.40 ± 9.80	24.96 ± 10.85	26.69 ± 10.611;@

Values are expressed as Mean ± SD. Significance:
* $p<0.05$.
** $p<0.01$, when compared with normotensive control women delivering male babies.
@ $p<0.05$.
@@ $p<0.01$ when compared with normotensive control women delivering female babies.

Table 4
Cord plasma fatty acids in different groups.

Fatty acid (g/100 g fatty acids)	Normotensive control (n=122)	Preeclampsia (n=90)
Myristic acid	0.73 ± 0.29	0.84 ± 0.26**
Myristoleic acid	0.04 ± 0.07	0.10 ± 0.16**
Palmitic acid	28.55 ± 3.42	29.20 ± 3.18
Palmitoleic acid	2.51 ± 0.83	2.98 ± 0.84**
Stearic acid	10.17 ± 2.53	10.20 ± 2.30
Oleic acid	14.64 ± 2.07	16.30 ± 2.48**
Linoleic acid	15.69 ± 7.93	15.25 ± 7.03
γ-Linolenic acid	0.33 ± 0.16	0.31 ± 0.10**
α-Linolenic acid	0.43 ± 0.16	0.34 ± 0.17**
Dihomo-γ-linolenic acid	2.34 ± 0.71	2.22 ± 0.69
Arachidonic acid	13.72 ± 4.42	12.22 ± 3.67
Eicosapentaenoic acid	0.34 ± 0.31	0.35 ± 0.39
Nervonic acid	1.07 ± 0.41	0.89 ± 0.36**
Docosapentaenoic acid	0.47 ± 0.22	0.29 ± 0.26*
Docohexaenoic acid	1.92 ± 0.85	1.68 ± 0.64*
Saturated fatty acids	39.45 ± 4.45	40.25 ± 3.95
Monounsaturated fatty acids	18.28 ± 2.24	20.27 ± 2.71**
Total n-3 fatty acids	2.69 ± 0.90	2.37 ± 0.75 *
Total n-6 fatty acids	32.57 ± 4.94	30.31 ± 5.23
n-6/n-3 ratio	13.83 ± 6.66	14.73 ± 7.99

Values are expressed as Mean ± SD. Significance:
* $p<0.05$.
** $p<0.01$, when compared with normotensive control.

levels of estrogens which are known to regulate the levels of desaturase enzymes [39].

Nervonic acid is an important monounsaturated omega-9 fatty acid in sphingomyelin and functions in the biosynthesis of nerve cell myelin in the brain [40]. The accretions of nervonic acid are a good marker to track myelinogenesis [41]. In our current study cord nervonic acid levels were lower in women with preeclampsia as compared with normotensive control. These lower levels of nervonic acid may affect the fetal brain growth and development in the preeclampsia group and may have long term consequences on brain functions. Assies et al. [42] have also reported lower plasma and erythrocyte nervonic acid levels in major depressive disorder patients [42]. Further, we observed lower cord levels of nervonic acid in women with preeclampsia delivering male babies but not in the female babies. Children born to mothers with preeclampsia are reported to have a greater risk for developing neurodevelopmental and metabolic disorders in later life [14,15]. Our data indicates that male babies may be at an increased risk for developing neurodevelopmental disorders.

We and others have shown a positive association between maternal DHA and AA status and baby birth outcome in different populations [43–46]. Recent studies indicate that maternal LCPUFA may serve as prenatal growth factors, while n-6 LCPUFA regulate postnatal growth [47].

Different environmental and hormonal factors have shown to be associated with many early onset neurodevelopmental disorders in males than females [48,49]. Prevalence of brain disorders like schizophrenia has been reported to be higher in men than in women [50]. Specifically, fetal growth is reported to be more impaired in male infants born to women with preeclampsia [51]. Similarly, studies indicate that risk of neurodevelopmental impairment is higher in male children born to mothers with preeclampsia [52].

In conclusion, our data indicate that altered levels of LCPUFA may have differential implications for the growth and development of infants born to women with preeclampsia. Future studies are needed to follow up these male and female babies and examine their associations with maternal and cord LCPUFA levels. This may be useful in planning early interventions to prevent risk for adult diseases in women with PE.

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Table 5
Cord plasma fatty acids in women delivering male and female babies.

Fatty acid (g/100 g fatty acids)	Normotensive control ($n=122$)		Preeclampsia ($n=90$)	
	Male ($n=69$)	Female ($n=53$)	Male ($n=54$)	Female ($n=36$)
Myristic acid	0.75 ± 0.31	0.70 ± 0.26	0.91 ± 0.26**	0.72 ± 0.22
Myristoleic acid	0.04 ± 0.09	0.03 ± 0.05	0.13 ± 0.19**	0.03 ± 0.05
Palmitic acid	27.95 ± 3.27	29.55 ± 3.48	29.28 ± 3.50	29.08 ± 2.61
Palmitoleic acid	2.50 ± 0.070	2.54 ± 1.02	2.94 ± 0.98*	3.04 ± 0.57
Stearic acid	10.30 ± 2.49	9.93 ± 2.63	10.04 ± 2.52	10.45 ± 1.89
Oleic acid	14.77 ± 2.15	14.43 ± 1.94	16.37 ± 2.45*	16.17 ± 2.58
Linoleic acid	15.25 ± 6.72	16.44 ± 9.71	16.04 ± 7.68	13.96 ± 5.86
γ-Linolenic acid	0.33 ± 0.17	0.34 ± 0.15	0.29 ± 0.10	0.32 ± 0.091;@
α-Linolenic acid	0.43 ± 0.17	0.42 ± 0.15	0.33 ± 0.18*	0.36 ± 0. 15
Dihomo-γ-linolenic acid	2.35 ± 0.68	2.33 ± 0.77	2.10 ± 0.68	2.41 ± 0.68
Arachidonic acid	14.06 ± 4.32	13.14 ± 4.61	11.73 ± 3.34*	13.03 ± 4.09
Eicosapentaenoic acid	0.32 ± 0.31	0.37 ± 0.33	0.29 ± 0.26	0.44 ± 0.53
Nervonic acid	1.16 ± 0.42$	0.93 ± 0.37	0.85 ± 0.37**	0.96 ± 0.35
Docosapentaenoic acid	0.50 ± 0.23	0.41 ± 0.20	0.29 ± 0.26**	0.29 ± 0.0271;@
Docohexaenoic acid	1.89 ± 0.73	1.97 ± 1.04	1.72 ± 0.65	1.60 ± 0.63
Saturated fatty acids	39.01 ± 4.45	40.19 ± 4.43	40.24 ± 4.31	40.26 ± 3.35
Monounsaturated fatty acids	18.48 ± 2.44	17.94 ± 1.83	20.31 ± 2.77*	20.21 ± 2.661;@
Total n-3 fatty acids	2.65 ± 0.83	2.77 ± 1.03	2.36 ± 0.72	2.40 ± 0.801;@
Total n-6 fatty acids	32.50 ± 4.50	32.68 ± 5.68	30.47 ± 5.64	30.04 ± 4.56
n-6/n-3 ratio	13.71 ± 5.67	14.03 ± 8.17	14.82 ± 8.35	14.59 ± 7.52

Values are expressed as Mean ± SD. Significance:

* $p < 0.05$ when compared with normotensive control women delivering male babies.

@ $p < 0.05$ when compared with normotensive control women delivering female babies.

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References

[1] N. Al-Jameil, F. Aziz Khan, M. Fareed Khan, H. Tabassum, A brief overview of preeclampsia, J. Clin. Med. Res. 6 (2014) 1–7.
[2] A.V. Kulkarni, S.S. Mehendale, H.R. Yadav, A.S. Kilari, V.S. Taralekar, S.R. Joshi, Circulating angiogenic factors and their association with birth outcomes in preeclampsia, Hypertens. Res. 33 (2010) 561–567.
[3] S. Mehendale, A. Kilari, K. Dangat, V. Taralekar, S. Mahadik, S. Joshi, Fatty acids, antioxidants, and oxidative stress in pre-eclampsia, Int. J. Gynaecol. Obstet. 100 (2008) 234–238.
[4] I. Cetin, G. Alvino, M. Cardellicchio, Long chain fatty acids and dietary fats in fetal nutrition, J. Physiol. 587 (2009) 3441–3451.
[5] E. Larqué, A. Gil-Sánchez, M.T. Prieto-Sánchez, B. Koletzko, Omega 3 fatty acids, gestation and pregnancy outcomes, Br. J. Nutr. 107 (2012) S77–S84.
[6] H. Lee, W.J. Park, Unsaturated fatty acids, desaturases, and human health, J. Med. Food 17 (2014) 189–197.
[7] R.A. Gibson, B. Muhlhausler, M. Makrides, Conversion of linoleic acid and alpha-linolenic acid to long-chain polyunsaturated fatty acids (LCPUFAs), with a focus on pregnancy, lactation and the first 2 years of life, Matern. Child Nutr. 7 (2011) 17–26.
[8] N.M. Abu-Ouf, M.M. Jan, The influence of fish oil on neurological development and function, Can. J. Neurol. Sci. 41 (2014) 13–18.
[9] M.A. Crawford, C.L. Broadhurst, M. Guest, et al., A quantum theory for the irreplaceable role of docosahexaenoic acid in neural cell signalling throughout evolution, Prostaglandins Leukot. Essent. Fatty Acids 88 (2013) 5–13.
[10] S.J. Carlson, E.M. Fallon, B.T. Kalish, K.M. Gura, M. Puder, The role of the ω-3 fatty acid DHA in the human life cycle, JPEN J. Parenter. Enter. Nutr. 37 (2013) 15–22.
[11] J.F. Gould, L.G. Smithers, M. Makrides, The effect of maternal omega-3 (n-3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials, Am. J. Clin. Nutr. 97 (2013) 531–544.
[12] E. Oda, K. Hatada, J. Kimura, Y. Aizawa, P.V. Thanikachalam, K. Watanabe, Relationships between serum unsaturated fatty acids and coronary risk factors: negative relations between nervonic acid and obesity-related risk factors, Int. Heart J. 46 (2005) 975–985.
[13] H. Yuan, Q.H. Wang, Y.Y. Wang, C.M. Xie, K.Q. Xie, X.L. Zhao, Effect of docosahexaenoic acid and nervonic acid on the damage of learning and memory abilities in rats induced by 1-bromopropane, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 31 (2013) 806–810.
[14] A. Fraser, S.M. Nelson, C. Macdonald-Wallis, N. Sattar, D.A. Lawlor, Hypertensive disorders of pregnancy and cardiometabolic health in adolescent offspring, Hypertension 62 (2013) 614–620.
[15] J.R. Mann, S. McDermott, Are maternal genitourinary infection and pre-eclampsia associated with ADHD in school-aged children? J. Atten. Disord. 15 (2011) 667–673.
[16] A. Many, A. Fattal, Y. Leitner, M.J. Kupferminc, S. Harel, A. Jaffa, Neurodevelopmental and cognitive assessment of children born growth restricted to mothers with and without preeclampsia, Hypertens. Pregnancy 22 (2003) 25–29.
[17] R.C. Knickmeyer, M. Davenport, Turner syndrome and sexual differentiation of the brain: implications for understanding male-biased neurodevelopmental disorders, J. Neurodev. Disord. 3 (2011) 293–306.
[18] S. Lohner, K. Fekete, T. Marosvölgyi, T. Decsi, Gender differences in the long-chain polyunsaturated fatty acid status: systematic review of 51 publications, Ann. Nutr. Metab. 62 (2013) 98–112.
[19] C.M. Sibbons, J.T. Brenna, P. Lawrence, et al., Effect of sex hormones on n-3 polyunsaturated fatty acid biosynthesis in HepG2 cells and in human primary hepatocytes, Prostaglandins Leukot. Essent. Fatty Acids 90 (2014) 47–54.
[20] T. Decsi, K. Kennedy, Sex-specific differences in essential fatty acid metabolism, Am. J. Clin. Nutr. 94 (2011) 1914S–1919S.
[21] C.E. Childs, M. Romeu-Nadal, G.C. Burdge, P.C. Calder, The polyunsaturated fatty acid composition of hepatic and plasma lipids differ by both sex and dietary fat intake in rats, J. Nutr. 140 (2010) 245–250.
[22] A. Wang, S. Rana, S.A. Karumanchi, Preeclampsia: the role of angiogenic factors in its pathogenesis, Physiology (Bethesda) 24 (2009) 147–158.
[23] S. Saito, A. Nakashima, A review of the mechanism for poor placentation in early-onset preeclampsia: the role of autophagy in trophoblast invasion and vascular remodeling, J. Reprod. Immunol. 101–102 (2014) 80–88.
[24] V.L. Clifton, Review: sex and the human placenta: mediating differential strategies of fetal growth and survival, Placenta 31 (2010) S33–S39.
[25] T. Prior, M. Wild, E. Mullins, P. Bennett, S. Kumar, Sex specific differences in fetal middle cerebral artery and umbilical venous Doppler, PLoS One 8 (2013) e56933.
[26] K.D. Dangat, S.S. Mehendale, H.R. Yadav, et al., Long-chain polyunsaturated fatty acid composition of breast milk in preeclamptic mothers, Neonatology 97 (2010) 190–194.
[27] V.A. D'Souza, A.S. Kilari, A.A. Joshi, S.S. Mehendale, H.M. Pisal, S.R. Joshi, Differential regulation of brain-derived neurotrophic factor in term and preterm preeclampsia, Reprod. Sci. 21 (2014) 230–235.
[28] A.V. Kulkarni, S.S. Mehendale, H.R. Yadav, S.R. Joshi, Reduced placental docosahexaenoic acid levels associated with increased levels of sFlt-1 in preeclampsia, Prostaglandins Leukot. Essent. Fatty Acids 84 (2011) 51–55.

[29] A.S. Kilari, S.S. Mehendale, K.D. Dangat, et al., Long chain polyunsaturated fatty acids in mothers and term babies, J. Perinatal Med. 37 (2009) 513–518.
[30] E.J. Giltay, L.J. Gooren, A.W. Toorians, M.B. Katan, P.L. Zock, Docosahexaenoic acid concentrations are higher in women than in men because of estrogenic effects, Am. J. Clin. Nutr. 80 (2004) 1167–1174.
[31] F.L. Crowe, C.M. Skeaff, T.J. Green, A.R. Gray, Serum n-3 long-chain PUFA differ by sex and age in a population-based survey of New Zealand adolescents and adults, Br. J. Nutr. 99 (2008) 168–174.
[32] G.C. Burdge, J.L. Slater-Jefferies, R.A. Grant, et al., Sex, but not maternal protein or folic acid intake, determines the fatty acid composition of hepatic phospholipids, but not of triacylglycerol, in adult rats, Prostaglandins Leukot. Essent. Fatty Acids 78 (2008) 73–79.
[33] A. Extier, B. Langelier, M.H. Perruchot, et al., Gender affects liver desaturase expression in a rat model of n-3 fatty acid repletion, J. Nutr. Biochem. 21 (2010) 180–187.
[34] G.C. Burdge, S.A. Wootton, Conversion of alpha-linolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women, Br. J. Nutr. 88 (2002) 411–420.
[35] R. Pawlosky, J. Hibbeln, Y. Lin, N. Salem, n-3 fatty acid metabolism in women (discussion 994-5), Br. J. Nutr. 90 (2003) 993–994.
[36] M.J. de Alaniz, C.A. Marra, Steroid hormones and fatty acid desaturases, Prostaglandins Leukot. Essent. Fatty Acids 68 (2003) 163–170.
[37] T.W. Flinsenberg, S. van der Sterren, A.N. van Cleef, M.J. Schuurman, P. Agren, E. Villamor, Effects of sex and estrogen on chicken ductus arteriosus reactivity, Am. J. Physiol. Regul. Integr. Comp. Physiol. 298 (2010) R1217–R1224.
[38] R. Tamimi, P. Lagiou, L.J. Vatten, et al., Pregnancy hormones, pre-eclampsia, and implications for breast cancer risk in the offspring, Cancer Epidemiol. Biomark. Prev. 12 (2003) 647–650.
[39] E.J. Giltay, L.J. Gooren, A.W. Toorians, M.B. Katan, P.L. Zock, Docosahexaenoic acid concentrations are higher in women than in men because of estrogenic effects, Am. J. Clin. Nutr. 80 (2004) 1167–1174.
[40] J.R. Sargent, K. Coupland, R. Wilson, Nervonic acid and demyelinating disease, Med. Hypotheses 42 (1994) 237–242.
[41] M. Martinez, Tissue levels of polyunsaturated fatty acids during early human development, J. Pediatr. 120 (1992) S129–S138.
[42] J. Assies, F. Pouwer, A. Lok, et al., Plasma and erythrocyte fatty acid patterns in patients with recurrent depression: a matched case-control study, PLoS One 5 (2010) e10635.
[43] N.S. Wadhwani, H.R. Pisal, S.S. Mehendale, S.R. Joshi, A prospective study of maternal fatty acids, micronutrients and homocysteine and their association with birth outcome, Matern. Child Nutr. (2013), http://dx.doi.org/10.1111/mcn.12062.
[44] L.J. Smits, H.M. Elzenga, R.J. Gemke, G. Hornstra, M. van Eijsden, The association between interpregnancy interval and birth weight: what is the role of maternal polyunsaturated fatty acid status? BMC Pregnancy Childbirth 13 (2013) 23.
[45] A. Kilari, S. Mehendale, H. Pisal, T. Panchanadikar, A. Kale, S. Joshi, Nerve growth factor, birth outcome and pre-eclampsia, Int. J. Dev. Neurosci. 29 (2011) 71–75.
[46] M. van Eijsden, G. Hornstra, M.F. van der Wal, T.G. Vrijkotte, G.J. Bonsel, Maternal n-3, n-6, and trans fatty acid profile early in pregnancy and term birth weight: a prospective cohort study, Am. J. Clin. Nutr. 87 (2008) 887–895.
[47] D. Much, S. Brunner, C. Vollhardt, et al., Effect of dietary intervention to reduce the n-6/n-3 fatty acid ratio on maternal and fetal fatty acid profile and its relation to offspring growth and body composition at 1 year of age, Eur. J. Clin. Nutr. 67 (2013) 282–288.
[48] A.S. Khashan, K.M. Abel, R. McNamee, et al., Higher risk of offspring schizophrenia following antenatal maternal exposure to severe adverse life events, Arch. Gen. Psychiatry 65 (2008) 146–152.
[49] R.C. Knickmeyer, M. Davenport, Turner syndrome and sexual differentiation of the brain: implications for understanding male-biased neurodevelopmental disorders, J. Neurodev. Disord. 3 (2011) 293–306.
[50] G.E. Gillies, S. McArthur, Estrogen actions in the brain and the basis for differential action in men and women: a case for sex-specific medicines, Pharmacol. Rev. 62 (2010) 155–198.
[51] S.A. Reynolds, J.M. Roberts, L.M. Bodnar, C.L. Haggerty, A.O. Youk, J.M. Catov, Newborns of women with preeclampsia show evidence of sex-specific disparity in fetal growth, Gend. Med. 9 (2012) 424–435.
[52] A. Spinillo, L. Montanari, B. Gardella, M. Roccio, M. Stronati, E. Fazzi, Infant sex, obstetric risk factors, and 2-year neurodevelopmental outcome among preterm infants, Dev. Med. Child Neurol. 51 (2009) 518–525.