Serum fatty acids are positively associated with changes in systemic blood pressure throughout pregnancy

Jaqueline Lepsch a, Dayana Rodrigues Farias a, Ilana Eshriqui a, Fernanda Rebelo b, Juliana dos Santos Vaz c, Amanda Amorim Adegboye d, Joseph R. Hibbeln e, Gilberto Kac a, * a Nutritional Epidemiology Observatory, Josué de Castro Nutrition Institute, Rio de Janeiro Federal University, Rio de Janeiro, RJ, Brazil b Clinical Research Division, Brazilian National Institute of Cancer, Rio de Janeiro, Brazil c Faculty of Nutrition, Federal University of Pelotas, Pelotas, RS, Brazil d Division of Nutrition, Food & Public Health, Department of Life Sciences, University of Westminster, London, United Kingdom e National Institute on Alcohol Abuse and Alcoholism, NIH, Rockville, United States

ARTICLE INFO

Keywords: Blood pressure Fatty acids Pregnancy Cohort study

Abstract

Objectives: To assess whether serum concentrations of saturated (SFAs), polyunsaturated (PUFAs), and mono-unsaturated (MUFAs) fatty acids are associated with changes in blood pressure (BP) throughout pregnancy.

Study design: Prospective cohort.

Main outcome measures: Longitudinal measurements of systolic (SBP) and diastolic (DBP) BP.

Methods: Two hundred twenty-three healthy pregnant women were recruited in a public health center in Rio de Janeiro, Brazil between 2009 and 2011. Fasting blood samples and BP measurements were obtained at the 1st (5th–13th weeks), 2nd (20th–26th) and 3rd trimester (30th–36th). Crude and adjusted (maternal age, education, energy intake, gestational body weight change, leptin concentrations, early pre-pregnancy BMI, leisure time physical activity prior to pregnancy and linear and quadratic gestational weeks) longitudinal linear mixed-effects models were employed.

Results: SBP and DBP decreased from the 1st to the 2nd trimester and slightly increased from the 2nd to the 3rd trimester (P < 0.001). In the adjusted model (β and 95% CI), total SFAs [0.005 (0.001–0.008); P = 0.008], total MUFAs [0.005 (0.001–0.009); P = 0.019] and total n-6 PUFAs [0.005 (0.001–0.009); P = 0.025] were positively associated with SBP throughout pregnancy.

Conclusions: Maternal serum concentrations of total SFAs, MUFAs and n-6 PUFAs were positively associated with BP levels in normotensive pregnant women.

1. Introduction

Physiological hemodynamic changes occur in the mother’s body during pregnancy to accommodate maternal and fetal demands. Adaptations of the cardiovascular system include decreased vascular resistance and increased blood volume and systolic (SBP) and diastolic (DBP) blood pressure (BP) [1,2]. Studies have reported that maternal SBP and DBP tend to decrease from the 1st to the 2nd trimester and later increase progressively until delivery in uncomplicated pregnancies [2,3].

Although these physiological adaptations are expected, BP levels are inversely associated with birth weight and gestational age at birth, even in normotensive women [4,5]. Given the importance of BP to the pregnancy outcome, efforts have been undertaken to elucidate factors that may influence changes in BP during pregnancy. There is a growing body of evidence supporting the hypothesis that poor placenta implantation, mediated by systemic inflammatory response and endothelial cells dysfunctions, accounts for hypertension during pregnancy [6].

Thus, maternal biomarkers associated with endothelial cell function and the inflammatory response has the potential to be related to BP changes during pregnancy [7]. Fatty acids (FAs) are important endocrine mediators that play a major role in the inflammatory process [8] and vascular function in the offspring [9] and may have different bioactive properties and functions depending on the number of unsaturated bonds [10]. Greater intakes and levels of saturated fatty acids (SFAs) have also been related with increased levels of low-density lipoproteins (LDL-cholesterol) [11], thereby potentially contributing to

https://doi.org/10.1016/j.preghy.2018.04.012
Received 17 July 2017; Received in revised form 23 February 2018; Accepted 11 April 2018
Available online 25 April 2018
2210-7789/ © 2018 International Society for the Study of Hypertension in Pregnancy. Published by Elsevier B.V. All rights reserved.
an increased risk of developing cardiovascular disease [12]. However, the results of a large randomized clinical trial (RCT) has cast doubt on this finding [13]. In addition, observational trials and RCTs have reported that higher intake of monounsaturated fatty acids (MUFAs) and n-3 polyunsaturated fatty acids (PUFAs) may contribute to a decrease in BP in adult populations [14,15].

It is well-known that serum concentrations of FAs are increased during pregnancy [16]. Furthermore, studies have shown a high FA requirement to ensure adequate embryo implantation and placenta development [6]. Recent studies have also shown differences in n-3 PUFA concentrations in different regions of the placenta among both normotensive pregnancies and women with preeclampsia [17,18]. An RCT that provided n-3 PUFAs as fish oils or fish meals have unequivocally demonstrated a reduction in BP [19]. Lim et al. (2015) observed an inverse association between maternal plasma concentrations of total n-3 PUFAs and peripheral SBP in a study with 751 Chinese, Malay and Indian pregnant women [20]. Intake of n-6 PUFAs has been associated with increased pro-inflammatory eicosanoid levels in the general population [21]. However, in vitro studies suggest that n-6 PUFA intake may facilitate the early placentaent process by stimulating angiogenesis in 1st trimester placental trophoblast cells [22,23,24].

Although there is previous evidence regarding the association between serum FAs and BP in the general population [14,15], we identified only one study that has investigated this association during pregnancy [20]. We aimed to investigate whether concentrations of various types of FAs during pregnancy were associated with BP throughout gestation in normotensive pregnant women. We hypothesized that during pregnancy, higher serum concentrations of MUFAs and n-3 PUFAs would be associated with lower SBP and DBP, while higher concentrations of SFAs and n-6 PUFAs would be associated with higher SBP and DBP values.

2. Methods

This report describes a prospective cohort study of pregnant women attending a prenatal care service offered by a public health center in Rio de Janeiro, Brazil. The enrollment of women occurred from November 2009 until October 2011, and the follow-up lasted until July 2012. The study consisted of three follow-up visits, which occurred during the 5th–13th (1st trimester), 20th–26th (2nd trimester), and 30th–36th (3rd trimester) gestational weeks.

A total of 322 women met the eligibility criteria [ < 13 gestational weeks; 20–40 years old; no chronic diseases (aside from obesity)] and were invited to participate. From those 322 women, 23 women chose not to participate, and 76 women were excluded after enrolment for the following reasons: were diagnosed with chronic diseases (n = 12) or with infectious diseases (n = 9), had advanced pregnancy (≥14 weeks of gestation) (n = 15), had multiple pregnancies (n = 4), missed the baseline interview (n = 5) or the baseline blood collection (n = 6) or suffered early miscarriages (n = 25). The baseline sample consisted of 223 pregnant women. From the baseline to the 2nd trimester visit, 19 additional exclusions occurred, and 15 follow-up losses occurred, with 189 women remaining at the 2nd trimester visit. Two women dropped out between the 2nd and 3rd visits. In addition, an RCT was nested within the cohort starting after the 2nd trimester and lasting until delivery. The RCT aimed to investigate the effect of n-3 PUFA supplementation on postpartum depression (ClinicalTrials.gov: NCT01660165). Forty-one out of 189 women were randomized and received six gelatin capsules per day containing fish oil (n = 20) or placebo (soybean oil, n = 21). Six women out of 41 did not adhere to the RCT and were analyzed at the 3rd trimester visit, while 35 women who adhered to the RCT were excluded from the 3rd trimester analysis with a final remaining sample of 152 women in the 3rd trimester (Fig. 1) [25].

2.1. Blood samples

Blood samples were obtained at the 1st (5th–13th weeks), 2nd (20th–26th) and 3rd trimester (30th–36th) after 12 h of fasting, and were collected in vacutainer tubes and immediately centrifuged (5,031 g for 5 min) within 1 h. Aliquots of serum (prepared from blood collected into tubes with a gel separator) were stored at −80 °C until analyses. Serum samples were used to determine the FA compositions.

2.2. Fatty acid concentrations

Analyses of serum FA composition were performed in the Section of Nutritional Neuroscience, Laboratory of Membrane Biochemistry and Biophysics of the National Institute of Health (NIH/USA). Serum samples were shipped from Brazil to the NIH/USA in boxes with dry ice.

High-throughput robotic direct methylation, coupled with fast gas-liquid chromatography, was used to identify the serum FAs. This technique was developed and validated by the NIH to allow analysis on a large scale [26]. The analyses were performed using a chromatograph HP 6890 Plus gas LAN equipped with three flame ionization detectors (Agilent Technologies, Santa Clara, CA, USA) coupled to a fused silica capillary column (Agilent 127-32H2 15 m × 0.1 mm × 0.1 mm).

Twenty-two FAs were measured: 14:0, 16:0, 16:1n-7, 18:0, 18:1n-9, 18:1n-7, 18:2n-6, 18:3n-6, 18:3n-3, 20:0, 20:1n-9, 20:2n-6, 20:3n-6, 20:4n-6, 20:5n-3, 22:0, 22:4n-6, 22:3n-3, 22:5n-3, 24:0, 22:6n-3, and 24:1n-9. Although we measured 22 FAs, we opted to present only n-3 and n-6 fractions plus totals for MUFAs, SFAs, and PUFAs, considering the representativeness of these fractions [27]. FAs were presented in absolute values (μg/mL).

2.3. Blood pressure

BP was measured twice at all follow-up visits (5th–13th, 20th–26th, and 30th-36th gestational weeks) with approximately 30-min intervals between measurements. The mean values obtained from each follow-up visit were calculated and considered in the analysis. Measurements were performed using an automated oscillometric BP monitoring system (Omron HEM-742, São Paulo, Brazil), which was previously validated [28] using an adequate cutoff that fit the upper arm’s circumference. Prior to measuring BP, women were asked to rest for at least five minutes and to be seated comfortably with their backs supported, legs uncrossed, and feet flat on the floor, remaining silent during the procedure. The arm with the cuff was supported at the heart level, with the palm facing up and the elbow slightly flexed.

2.4. Covariates assessment

A structured questionnaire was administered by trained interviewers at each pregnancy trimester to determine the women’s sociodemographic and lifestyle characteristics, including age (years), education (years), and practice of leisure time physical activity prior to pregnancy (yes/no). Total energy intake (kcal/d) was obtained using a validated food frequency questionnaire (FFQ), which used the previous six months’ pregnancy as the time frame. The FFQ was administered at baseline [29].

Weight was measured in each visit using an electronic scale (Filizzola Ltd., São Paulo, Brazil), calibrated to the nearest gram. Height was measured in duplicate using a portable stadiometer (Seca Ltd., Hamburg, Germany) at baseline. Early pregnancy body mass index (BMI) [weight (kg)/height (m²)] was determined based on the weight and height measured before the 13th gestational week. Women were classified according to early pregnancy BMI as either normal weight (18.5 < BMI ≤ 24.9 kg/m²), overweight (25 ≤ BMI ≤ 29.9 kg/m²), or obese (BMI > 30 kg/m²). Trained staff performed anthropometric measures using standardized procedures [30].

Gestational age was estimated by ultrasound if performed prior to
24 gestational weeks (n = 221). Otherwise, the reported date of the last menstrual period was used to calculate the gestational age (n = 2).

Plasma leptin concentrations were determined using a human-specific enzyme-linked immunosorbent assay (ELISA) method (Millipore, St. Charles, Missouri, USA) with a sensitivity of 0.5 ng/dl. All procedures were performed following the manufacturer’s instructions in duplicate.

2.5. Statistical analysis

The Shapiro–Wilk W-test was the statistical procedure used to assess the normality of the variables. We compared the mean concentrations of FAIs and the socio-economic profiles of pregnant women that reached the final follow-up (n = 152) with those that were considered losses of follow-up or exclusions (all combined, n = 71) using the chi-square test for categorical variables and Student’s t-test for continuous variables.

The women’s general characteristics were described with the mean and standard deviation. Mean SBP and DBP throughout pregnancy were compared using ANOVA for repeated measures. The mean values of SBP and DBP throughout pregnancy were calculated according to baseline tertiles of the FA (µg/mL) distribution. We also adopted tertiles because there are no established cut-off points for FA distribution. In each trimester of pregnancy, we compared the mean in each tertile of SBP and DBP using ANOVA. The Bonferroni test was employed as the main post hoc test to compare means of SBP and DBP in each trimester according to baseline FA tertiles (P-value < 0.05) [31].

Longitudinal linear mixed-effects (LME) regression models were performed to evaluate the association between FA concentrations and BP changes during pregnancy. The LME models capture inter- and intra-individual changes, considering that repeated measures of the same individual are correlated, and the models accommodate time-dependent and independent covariates and enable non-equidistant intervals [32]. Bivariate models were adjusted for gestational age (linear and quadratic). Quadratic gestational week was considered due to the parabolic BP pattern of variation during pregnancy. All models were fitted using the unstructured covariance matrix for random effects (intercept and slope). Confounders were added to the model based on biological plausibility and statistical significance in bivariate regression models (P < 0.2) with both the main exposure, FA concentrations, and outcome BP. Multivariate models were later adjusted for maternal age, education, energy intake, gestational body weight change, leptin concentrations, early pre-pregnancy BMI, leisure time physical activity prior to pregnancy and linear and quadratic gestational weeks. The residual distribution of the multiple longitudinal models was confirmed using scatter and quantile-quantile plots of residuals and plots to check the potential autocorrelation structure. We performed independent models for each serum FA.

Effect plots containing data scatter, longitudinal prediction, and 95% confidence intervals (CIs) were constructed to illustrate the variation in SBP and DBP during pregnancy according to tertiles of total SFAs, MUFRAs, and n-3 and n-6 PUFAs.

Stata Data Analysis, version 12.0 (Stata Corp., College Station, Texas, USA), and R statistical software package, version 3.1.2 were used to perform the statistical analyses.

2.6. Ethical approval

The Ethics Committee of the Maternity Hospital (protocol: 0023.0.361.00-08) and Institute of Psychiatry (protocol: 0012.0.249.000-09) from the Rio de Janeiro Federal University approved the study protocol. The Ethics Committee of the Municipal Secretary of Rio de Janeiro City also approved the study (protocol: 0139.0.314.000-09). All women provided their written informed consent (see Table 1).
and DBP (mean values of SBP in the 1st trimester (P = 0.03) compared to those classified in the 1st tertile at the 3rd trimester. However, no associations were observed regarding FA profiles concentrations and SBP (OR: 0.51, 95%CI: 0.92 to 0.93), even after adjusting for maternal age, ethnicity, education level, exercise, smoking, alcohol intake before or during pregnancy, BMI, gestational diabetes, heart rate and use of fish oil supplements [20].

Adequate FA levels during the prenatal and early periods of pregnancy are essential for placenta development and to maintain maternal concentrations. Severe deficits may have permanent effects if they occur during critical periods of early development [2,21]. FAOs are biologically active components that regulate placental angiogenesis, inflammation, and oxidative stress [23,37].

A strength of this study lies in its novelty. To the best of our knowledge, this report describes the first longitudinal study to investigate the association between serum FAAs and BP during pregnancy. Moreover, our longitudinal design and the robustness of the statistical analysis allowed us to assess BP and FA concomitant changes throughout the gestational period and to consider the data as repeated measures [32]. Another strength is the use of serum compositions of FAAs, which is considered to be more accurate than dietary data assessed in previous studies with FFQ [14,15]. The study participants’ losses to follow-up (7.6%) might be a study limitation, although these losses are expected in prospective studies. However, we observed that these losses were randomly distributed for the variables of interest. Furthermore, because women were excluded from our sample if they developed hypertension (n = 2), the association between FAAs levels and BP in this analysis may have been relatively weakened. Nevertheless, it is worth mentioning that we were able to show statistically significant associations between FAAs and BP, even considering only normotensive women. This information adds relevant knowledge in the context of prevention of gestational hypertensive disorders.

In conclusion, the present study observed that total serum SFAs were positively associated with SBP pregnancy. We also observed that

**Table 1**

<table>
<thead>
<tr>
<th>General characteristics of women.1</th>
<th>n</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>223</td>
<td>26.6 ± 5.4</td>
</tr>
<tr>
<td>Education, y</td>
<td>223</td>
<td>8.6 ± 2.9</td>
</tr>
<tr>
<td>Per-capita family income, US$2</td>
<td>216</td>
<td>311.7 ± 190.5</td>
</tr>
<tr>
<td>Early body mass index, kg/m²3</td>
<td>223</td>
<td>24.8 ± 4.8</td>
</tr>
<tr>
<td>Total gestational weight gain, kg4</td>
<td>201</td>
<td>13.0 ± 5.6</td>
</tr>
<tr>
<td>Energy intake, kcal/d</td>
<td>223</td>
<td>2,407 ± 886</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Systolic blood pressure, mmHg</th>
<th>n</th>
<th>All</th>
<th>P1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester</td>
<td>223</td>
<td>110.2 ± 9.2</td>
<td>0.04</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>189</td>
<td>108.9 ± 9.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>152</td>
<td>111.2 ± 9.6</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diastolic blood pressure, mmHg</th>
<th>n</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester</td>
<td>223</td>
<td>67.1 ± 7.6</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>189</td>
<td>65.0 ± 6.7</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>152</td>
<td>66.8 ± 7.2</td>
</tr>
</tbody>
</table>

1 Values are means ± standard deviation.

2 Variables with missing values.

3 P refers to comparison of means with ANOVA for repeated measures.

3. Results

No differences were observed regarding FA profile concentrations and other co-variables among women who completed the follow-up compared to those classified as lost to follow-up (Supplemental Table 1).

The mean SBP values presented similar trends according to tertiles of total SFAs concentrations throughout pregnancy. We observed a decrease from the 1st to the 2nd trimester and an increase at the 3rd trimester. However, those women classified in the 3rd tertile had higher mean values of SBP in the 1st trimester (P = 0.048) and 3rd trimester (P = 0.04) compared to those in the 1st and 2nd tertiles. Women in the 3rd tertile of total PUFAs n-6 also had higher means of SBP (P = 0.03) and DBP (P = 0.03) compared to those classified in the 1st tertile at the 1st trimester. At the 1st pregnancy trimester, higher DBP was associated with total n-3 PUFA tertiles (P = 0.04) but not during the 2nd or 3rd trimesters (Supplemental Tables 2 and 3).

Women in the 3rd tertile of total SFAs and total n-6 PUFAs had significantly higher SBP throughout pregnancy compared to women in the 1st tertile. Similar associations were found for DBP (Fig. 2).

The concentrations of total SFAs, MUFA and n-6 PUFAs were positively and significantly associated with SBP during pregnancy in both crude and adjusted models. However, no associations were observed with DBP (Table 2).

4. Discussion

The present study has two primary findings. First, we observed that total SFAs, total MUFA and total n-6 PUFAs concentrations were positively associated only with SBP. These analyses remained statistically significant after adjustment for potential confounders, such as maternal age, education, energy intake, gestational body weight change, leptin concentrations, early pregnancy BMI, leisure time physical activity prior to pregnancy and linear and quadratic gestational weeks. Second, we observed that pregnant women who classified into the highest tertile of SFAs (values ≥ 779.4 µg/mL) at baseline had significantly higher SBP and DBP values in the 1st trimester and 3rd trimester compared to those in the 1st and 2nd tertiles.

Total SFAs were positively and significantly associated with SBP. The receptors are consistent with a retrospective study involving 55 middle-aged adults studied by Kim et al. [33]. These authors observed that total SFAs, 14:0, 16:0, and 18:0 were positively and significantly correlated with SBP and DBP [33]. In addition, studies conducted with animals and humans have reported that SFAs concentrations play an important role on the regulation of endothelial function [8,9]. We suspect that this mechanism could partially explain our results. While the etiology of gestation hypertension remain unclear, our results may contribute to the elucidation of factors associated with BP changes throughout pregnancy.

We also observed that MUFA concentrations were positively associated with SBP levels during pregnancy. To the best of our knowledge, no previous studies have reported this longitudinal association among pregnant women. Among adult non-pregnant populations, previous observational and RCT studies reported contrasting results compared to our study, i.e., a higher intake of MUFA contributed to the control of BP and prevention of hypertension in adult populations [14]. Miura et al. [14] observed a significant inverse relationship of total MUFA intake with DBP in a sample of 4680 male and female adults (−0.82 mm Hg) from China, Japan, the UK, and the USA. In contrast, a significant increase of 1.70 mm Hg in DBP was found for those who were not following a special diet, did not consume nutritional supplements and were not diagnosed with chronic disease. Several other studies have shown similar results in the general population [34,35] as the ones presented by Miura et al. [14]. The lack of consensus for the above association may be partially explained because different types of designs were used. Furthermore, it is possible that in observational studies, such as the current one, the endogenous production of carbohydrates and the excess of calorie intake is the MUFA source, and the increased intake of MUFA may have beneficial effects [35].
Fig. 2. Longitudinal prediction of SBP and DBP levels according to tertiles of FAs during pregnancy. A - Total saturated fatty acids. B - Total monounsaturated fatty acids. C - Total n-6 fatty acids. D - Total n-3 fatty acids. Note: Fatty acids were categorized in tertiles of the sample distributions and 1st tertile was the reference category. The models were adjusted for age, education, energy intake, gestational body weight change, leptin concentrations, pre-pregnancy BMI, leisure time physical activity, linear and quadratic gestational weeks. Data are presented as linear mixed effect coefficient ($\beta$) and 95% CI. $P$ refers to the maximum likelihood estimator. A - SBP: 2nd tertile $\beta = 1.8 (-0.6-4.3), P = 0.146$; 3rd tertile $\beta = 2.6 (0.2-5.1), P = 0.033$. DBP: 2nd tertile $\beta = 2.0 (0.1-4.0), P = 0.042$; 3rd tertile $\beta = 1.8 (-0.1-3.8), P = 0.064$. B - SBP: 2nd tertile $\beta = 1.9 (-1.7-5.5), P = 0.312$; 3rd tertile $\beta = 1.4 (-1.1-3.9), P = 0.276$. DBP: 2nd tertile $\beta = 1.5 (-0.5-3.5), P = 0.135$; 3rd tertile $\beta = 0.6 (-1.4-2.6), P = 0.574$. C - SBP: 2nd tertile $\beta = 1.7 (-0.7-4.1), P = 0.165$; 3rd tertile $\beta = 2.5 (0.1-4.9), P = 0.045$. DBP: 2nd tertile $\beta = 1.7 (-0.2-3.7), P = 0.083$; 3rd tertile $\beta = 1.8 (-0.1-3.8), P = 0.068$. D - SBP: 2nd tertile $\beta = -1.3 (-3.7-1.1), P = 0.296$; 3rd tertile $\beta = 1.4 (-1.1-3.9), P = 0.264$. DBP: 2nd tertile $\beta = -0.99 (-2.9-1.0), P = 0.346$; 3rd tertile $\beta = 1.0 (-1.0-3.0), P = 0.352$. J. Lepsch et al. Pregnancy Hypertension 13 (2018) 7–13.
the total SFAs, total MUFAs and total n-6 PUFAs were positively and significantly associated with SBP. Given the importance of gestational hypertensive disorders to maternal and fetal health and given the scarcity of studies investigating this association, efforts should be undertaken to elucidate factors that may influence changes in BP during pregnancy.

5. Disclosure

The authors declare that they have no conflicts of interest.

Acknowledgments

This study received funding from the Research Foundation of the State of Rio de Janeiro (FAPERJ, grant number: E-26/111.400/2010, E-14/2010) and the National Council for Scientific and Technological Development (CNPq, grant number: 471196/2010-0). The PhD exchange program was funded with the grant number 401314/2014-6 from National Council for Scientific and Technological Development (CNPq).

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at https://doi.org/10.1016/j.preghy.2018.04.012.

References

gestation in women of Chinese, Malay, and Indian ethnicity, Medicine 94 (9) (2015)
c571.

actions and possible needs in relation to eicosanoid synthesis, J. Nutr. Biochem. 1
(3) (1990) 123-141.

[22] G.M. Johnsen, S. Basak, M.S. Weedon-Fekjaer, A.C. Staff, A.K. Duttaroy,
Docosahexaenoic acid stimulates tube formation in first trimester trophoblast cells,

[23] A.K. Duttaroy, S. Basak, Docosahexaenoic acid and angiogenesis: a role in early

[24] Basak, A.K. Duttaroy, Effects of fatty acids on angiogenic activity in the placental
exivillious trophoblast cells, Prostaglandins Leukot. Essent. Fatty Acids 88 (2)

[25] J. Vaz, D.R. Farias, A Omega-3 supplementation from pregnancy to postpartum to
prevent depressive symptoms: a randomized placebo-controlled trial, BMC

L.R. Goldman, J.R. Hibbels, Automated high-throughput fatty acid analysis of
umbilical cord serum and application to an epidemiological study, Lipids 47 (5)

K.G. Parhofer, B. Koletzko, J. Seissler, A. Lechner, Di-
ff
ferences in the serum non-
esterified Fatty Acid pro
fi
le of young women associated with a recent history of

[28] A. Coleman, P. Freeman, S. Steel, A. Shennan, Validation of the Omron MX3 Plus
oscillometric blood pressure monitoring device according to the European Society
of Hypertension international protocol, Blood Pressure Monit. 10 (3) (2005)
165–168.

[29] R. Sichieri, J.E. Everhart, Validity of a Brazilian food frequency questionnaire
against dietary recalls and estimated energy intake, Nutr. Res. 18 (1998)
1649–1659.


[32] J.D. Singer, J.B. Willett, Applied Longitudinal Data Analysis: Modeling Change and

saturated fatty acids and fatty acid desaturase indices in erythrocyte in middle-aged

[34] L. Schwingshackl, B. Strasser, G. Hoffmann, Effects of monounsaturated fatty acids
Metab. 59 (2-4) (2011) 176–186.

monounsaturated fatty acids and cardiovascular disease risk: a mini review, Lipids


[37] L. Mu, K.J. Mukamal, A.Z. Naqvi, Erythrocyte saturated fatty acids and systemic