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Changes in Serum Fatty Acids Levels during Pregnancy and After Delivery in a Longitudinal Study

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Abstract

Introduction: During pregnancy, several maternal metabolic adaptations occur. One of these adaptations is the significant changes in lipid metabolism which contribute to the nutrient balance of the fetal-placental unit, essential for fetal development and lactation.

Methods: In this study, serum concentration of different fatty acids in healthy pregnant women and three months postpartum were determined by capillary gas chromatography and compared to healthy non-pregnant women and men. Differences between groups were assessed with one-way analyses of variance and the post hoc Tukey-HSD test for multiple comparisons. The Mann-Whitney U test was used when a variable was not normally distributed. All statistical analyses were conducted using R statistical Software (version 3.3.1).

Results: The results showed that serum levels of these maternal fatty acids increased significantly from the middle until the end of pregnancy compared to non-pregnant women and decreased at postpartum. Saturated fatty acids were observed to contribute to the highest percentage of total serum fatty acids during gestation, followed by polyunsaturated and monounsaturated fatty acids. Additionally, serum levels of total, saturated, monounsaturated, polyunsaturated and TRAN's fatty acids were significantly elevated in healthy non-pregnant women when compared with men.

Conclusion: There are significant differences in the lipid profiles among pregnant and non-pregnant women and men, with a decrease in the serum profile of all fatty acids in the postpartum period.

Keywords: Pregnancy, Lipids, Fatty acids

Abbreviations: ARA: Arachidonic Acid; DHA: Docosahexaenoic Acid; DGLA: Dihomo- γ -linolenic Acid; HDL: High-density Lipoprotein; HOMA: Homeostasis Model Assessment; IR: Insulin Resistance; LDL: Low-density Lipoprotein; LPL: Lipoprotein Lipase; MUFA: Monounsaturated Fatty Acids; PUFA: Polyunsaturated Fatty Acids; SFA: Saturated Fatty acids; VLDL: Very Low-density Lipoprotein

Introduction

Pregnancy is characterized by changes in the maternal lipid metabolism, which has been divided into two phases, anabolic and catabolic. During the early gestational phase, adipose tissue deposits increase significantly due to the action of insulin. Towards the end of this period, due to insulin resistance and the effect of estrogen, hypertriglyceridemia and an increase in lipolysis in adipose tissue [1]. Furthermore, it has been shown that pregnant women with high insulin resistance are more likely to develop preeclampsia [2].

Additionally, during pregnancy there is a significantly increase of mass of adipose tissue for first and second trimesters [1]. In this way, during the early anabolic phase of pregnancy, in the adipose tissue occurs an increase in the activity of lipoprotein lipase (LPL), which contributes to the accumulation of maternal lipids deposits [2]. However, towards the end of pregnancy, when a catabolic phase predominates, maternal adipose tissue LPL activity decreased, triglyceride synthesis in maternal deposits are reduced and adipose tissue lipolysis results in an increase in circulating maternal free fatty acids and triglyceride levels [2].

Thus, fatty acids play an important role during fetal growth and development, as well as immunological functions, coordination of intracellular and extracellular communications and fundamental roles of cell function [3]. Given the importance of fatty acids throughout pregnancy, for both the mother and fetus, the objective of the present study is to determine by capillary gas chromatography the serum concentration of different fatty acids in healthy pregnant women during the three periods of pregnancy and three months after delivery. Furthermore, serum concentrations of these fatty acids determined throughout gestation were compared with serum levels of the same fatty acids in eumenorrheic healthy women and men.

Materials and Methods

Subjects

Patients in this study were recruited by the Obstetrics and Gynecology service of a public hospital (Hospital de Engativa ESE II Nivel) in Bogota, Colombia between 2012 and 2014. All pregnant women were interrogated for their complete medical history and were subjected to physical examination and routine laboratory analysis. Additionally, 50 young healthy non-pregnant women and 48 young healthy adult men were recruited in the study.

Women with hormonal diseases, hypothyroidism, hyperthyroidism, diabetes mellitus (in any moment), hypertension, previous pregnancy losses, on medications, drugs and/or alcohol abuse, or with chronic diseases were excluded.

We conducted a longitudinal prospective study nested within a cohort study of 475 pregnant women. Fatty acids concentrations were analyzed during three stages of pregnancy [first: 12.3 (11.9-12.6); second: 24.3 (24.1-24.5); third: 34.6 (34.2-35.3) weeks] up to three months after delivery in maternal serum of 100 healthy women, randomly selected from the cohort study described above. Gestational age was determined by the date of last menstrual period and first-trimester ultrasonography.

Ethics approval and consent to participate

This project was approved by the ethics committee of the School of Medicine of the National University of Colombia, in accordance with the Declaration of Helsinki. All subjects provided written informed consent to participate.

Biochemical and serum fatty acids analysis

Participant blood samples for biochemical determination were drawn following an overnight fast (between 07:00-08:00 H) from the antecubital vein into Vacutainer tubes. Serum samples were centrifuged at 3,000×g for 5 minutes 4°C, distributed in aliquots and stored at -80°C until measurements. Serum levels of cholesterol, total and HDL, triglycerides, glucose, and PCR were determined using commercially available kits (SPIN-React 120, Sant Esteve De Bas, and Spain). Serum insulin concentration was determined on a Roche Elecsys 2010 analyzer (Elecsys 2010, Roche Diagnostics, Germany). Insulin resistance (IR) was analyzed by the Homeostasis Model Assessment (HOMA). Serum progesterone levels were analyzed in healthy non-pregnant women during the follicular and luteal phases of the menstrual cycle, using the electrochemiluminescence detection system (Roche, Progesterone Assay-Elecsys).

Lipids were extracted from 0.2 ml serum with chloroform/methanol after addition of an internal standard (methyl tridecanoate) using a modified Folch method [4]. Total lipids (cholesterol ester, phospholipids, triacylglycerol's and free fatty acids) were transmethylated with BF₃-methanol (14%) [5]. The resultant fatty acid methyl esters were extracted with hexane and injected by an auto-sampler into a 7890A gas chromatograph (Agilent Technologies, Palo Alto, CA, USA) in pulsed split less injection mode. GC was equipped with a flame-

ionization detector. The fatty acid methyl esters were separated on a 100 m × 0.25 mm, film thickness: 0.20 µm (Supelco) capillary column. Fatty acid methyl esters were identified by comparison with authentic standards (Nu-Chek-Prep, Minnesota, USA). Blank extractions were analyzed to correct for background contamination. The fatty acids were expressed in absolute concentrations (mg FA/dL serum).

Additionally, an overview of the systemic names and abbreviations of the fatty acids of each group analyzed appears in Supplementary table 1. The poly-unsaturated fatty acids (PUFA) correspond to the sum of Omega-3 and Omega-6 fatty acids. Total fatty acid concentration is the sum of saturated fatty acids (SFA), mono-unsaturated fatty acids (MUFA), PUFA, and TRANS fatty acids (TFA). Non-pregnant healthy women and men were used as control.

Statistical analysis

Data are presented as mean ± SD (standard deviation) or median (inter-quartile range). Differences between groups were assessed with one-way analyses of variance and the post hoc Tukey-HSD test for multiple comparisons. The Mann-Whitney U test was used when a variable was not normally distributed. Significance was accepted at $p < 0.05$. All statistical analyses were conducted using R statistical Software (version 3.3.1).

Results

Table 1 shows the demographic, biochemical and hormonal characteristics of the study subjects. Additionally, all serum fatty acid concentrations determined by capillary gas chromatography are shown in Supplementary table 2.

As observed in table 1, there are no significant age differences ($p > 0.05$) in the men, non-pregnant and healthy pregnant women. Additionally, an increase was observed throughout gestation in serum levels of triglycerides ($p < 0.05$), total cholesterol ($p < 0.05$), HDL ($p < 0.05$), insulin ($p < 0.05$), as previously reported [6]. Serum levels of C-reactive protein are elevated during the three trimesters of gestation studied when compared with the group of non-pregnant healthy women and men ($p < 0.05$) (Table 1).

The fatty acid concentrations are expressed as serum mg/dL in Supplementary table 2. Serum profile and percentage frequency distribution of SFA (Figure 1A and 1B and Supplementary Table 2), MUFA (Figure 2A and 2B, and Supplementary Table 2), PUFA (Figure 3A and 3B, and Supplementary Table 2), TFA (Figure 4A

and 4B, and Supplementary Table 2), Omega-3 fatty acids (Supplementary Figure 1A and 1B, Supplementary Table 2) and Omega 6 fatty acids (Supplementary Figure 2A and 2B, Supplementary Table 2), are represented during pregnancy and postpartum.

With regard to SFA, these fatty acids serum levels differ ($p < 0.05$) between men, healthy non-pregnant women, women during the three trimesters of gestation and in postpartum (Figure 1, and Supplementary Table 2). The SFA serum level profile is elevated ($p < 0.05$) in pregnant women, when compared to non-pregnant women ($p < 0.05$). SFA serum levels in men are lower when compared to the different study groups ($p < 0.05$) (Figure 1). Among the members of SFA, lauric acid serum levels were elevated in non-pregnant women when compared to men ($p < 0.05$) (Supplementary Table 2). Lauric acid serum levels were elevated in pregnant women in the first trimester when compared with non-pregnant women ($p < 0.05$) (Supplementary Figure 4A). Lauric acid serum levels decrease towards the end of gestation and remain low in three months. Postpartum when compared to first trimester women ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 4A). Additionally, myristic acid serum levels are higher in the second and third trimesters of gestation when compared against the other groups ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 4B).

With respect to pentadecanoic acid, serum levels rise from the first trimester when compared to healthy non-pregnant women and three months postpartum women ($p < 0.05$) (Supplementary Table 2). Similarly, palmitic acid serum levels rise significantly from the first trimester and are higher in the third trimester when compared with those of non-pregnant women ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 4C). Margaric acid serum levels rise in the second trimester when compared with the other groups of women ($p < 0.05$) (Supplementary Table 2). Serum levels of stearic acid were elevated in the third trimester ($p < 0.05$) (Supplementary Table 2). Serum Arachidic acid levels decrease in the first and second trimesters ($p < 0.05$) and in the third trimester are again equal to those of non-pregnant women (Supplementary Table 2, Supplementary Figure 4D). Behenic acid is the only fatty acid in the SFA group in which serum levels are elevated in men when compared with non-pregnant women ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 4E). Serum levels of behenic acid decrease in the first trimester and from the second trimester rise until the end of gestation ($p < 0.05$) (Supplementary Table

2, Supplementary Figure 4E). These serum levels do not decrease in the postpartum to the levels of non-pregnant women. Lignoceric acid was not detected in the first trimester of gestation ($p < 0.05$) (Supplementary Table 2). In most cases, male SFA serum levels are lower when compared to serum levels of women in the different groups ($p < 0.05$) (Supplementary Table 2). Overall, SFA serum levels decrease postpartum ($p < 0.05$) (Supplementary Table 2).

myristic acid, pentadecylic acid, margaric acid, arachidic acid, behenic acid and lignoceric acid) respect to the mean serum concentration of SFA in the different groups of subjects studied. SFA: saturated fatty acids.

In the study, MUFA serum levels differed among the groups analyzed ($p < 0.05$) (Figure 2 and Supplementary Table 2). Serum levels of MUFA are lower in men when compared with those of non-pregnant women ($p < 0.05$). Also, MUFA serum levels decreased during the first trimester compared to non-pregnant women ($p < 0.05$). Later, from the second trimester, MUFA serum levels rise compared to that of non-pregnant women, becoming higher in the third trimester ($p < 0.05$) (Figure 2 and Supplementary). Finally, at three months postpartum, serum levels of MUFA are lower when compared with women in the first trimester and non-pregnant women ($p < 0.05$) (Figure 2 and Supplementary Table 2). Palmitoleic and gadoleic acid have serum profiles similar to MUFA, with lower serum levels in men compared with non-pregnant women ($p < 0.05$) (Supplementary Table 2). Palmitoleic and gadoleic acid serum levels rise during pregnancy, are higher at the end of gestation and then decrease by three months postpartum ($p < 0.05$) (Supplementary Table 2).

Figure 1: Concentrations of SFA during pregnancy, postpartum and in a group of men and non-pregnant women. A. Box-and-whisker plot with median value, interquartile range, and lower and upper values of serum concentrations of SFA in six groups of subjects: men ($n = 48$), women ($n = 50$), pregnant women in first trimester ($n = 100$), second trimester ($n = 100$), third trimester ($n=100$) and 3 months postpartum ($n = 100$). *Women during pregnancy and postpartum had a longitudinal follow-up. Men = M; Women = W; F = Trimester I; S = Trimester II; T = Trimester III; 3 months postpartum = P. A p -value < 0.05 was considered statistically significant. The letter or letters (M, W, F, S, T and P) under each box-and whisker plot indicate against which group there were no statistically significant differences; if there is only one letter indicates that the group was statistically different from the other groups. B. Percentage of palmitic acid, stearic acid and other saturated fatty acids (lauric acid,

Figure 2: Concentrations of MUFA during pregnancy, postpartum and in a group of men and non-pregnant women. A. Box-and-whisker plot with median value,

interquartile range, and lower and upper values of serum concentrations of MUFA in six groups of subjects: men (n = 48), women (n = 50), pregnant women in first trimester (n = 100), second trimester (n = 100), third trimester (n = 100) and 3 months postpartum (n = 100). *Women during pregnancy and postpartum had a longitudinal follow-up. Men = M; Women = W; F = Trimester I; S = Trimester II; T = Trimester III; 3 months postpartum = P. A p-value < 0.05 was considered statistically significant. The letter or letters (M, W, F, S, T and P) under each box-and whisker plot indicate against which group there were no statistically significant differences; if there is only one letter indicates that the group was statistically different from the other groups. B. Percentage of palmitoleic acid, oleic acid and other monounsaturated fatty acids (gadoleic acid, erucic acid and nervonic) respect to the mean serum concentration of MUFA in the different groups of subjects studied. MUFA: monounsaturated fatty acids.

Figure 3: Concentrations of PUFA during pregnancy, postpartum and in a group of men and non-pregnant women. A. Box-and-whisker plot with median value, interquartile range, and lower and upper values of serum concentrations of PUFA in six groups of subjects: men (n = 48), women (n = 50), pregnant women in first trimester (n = 100), second trimester (n=100), third trimester (n=100) and 3 months postpartum (n = 100). *Women during pregnancy and postpartum had a longitudinal

follow-up. Men = M; Women = W; F = Trimester I; S = Trimester II; T = Trimester III; 3 months postpartum = P. A p-value < 0.05 was considered statistically significant. The letter or letters (M, W, F, S, T and P) under each box-and whisker plot indicate against which group there were no statistically significant differences; if there is only one letter indicates that the group was statistically different from the other groups. B. Percentage of linoleic acid, arachidonic acid (ARA) and other polyunsaturated fatty acids (γ-Linolenic acid, α-Linolenic acid, eicosadienoic acid, dihomo-γ-linolenic acid, eicosapentanoic acid (EPA), docosadienoic acid and docosahexanoic acid) respect to the mean serum concentration of PUFA in the different groups of subjects studied. PUFA: polyunsaturated fatty acids.

Figure 4: TRAN's fatty acids during pregnancy, postpartum and in a group of men and non-pregnant women. A. Box-and-whisker plot with median value, interquartile range, and lower and upper values of serum concentrations of trans fatty acids in six groups of subjects: men (n = 48), women (n = 50), pregnant women in first trimester (n = 100), second trimester (n = 100), third trimester (n = 100) and 3 months postpartum (n = 100). *Women during pregnancy and postpartum had a longitudinal follow-up. Men = M; Women = W; F = Trimester I; S = Trimester II; T = Trimester III; 3 months postpartum = P. A p-value < 0.05

was considered statistically significant. The letter or letters (M, W, F, S, T and P) under each box-and whisker plot indicate against which group there were no statistically significant differences; if there is only one letter indicates that the group was statistically different from the other groups. B. Percentage of elaidic acid, linoleic acid and α -linolenic acid (all-trans-9,12,15-Octadecatrienoic acid) respect to the mean serum concentration of TRAN's fatty acids in the different groups of subjects studied.

With respect to oleic acid, serum levels are diminished in the first trimester compared to serum levels of non-pregnant women and then rise in the second and third trimesters, to later decrease in the three months postpartum ($p < 0.05$) (Supplementary Table 2). Erucic acid rises significantly at the beginning of pregnancy while being similar to the rest of the groups (Supplementary Table 2). Nervonic acid serum levels are similar between men and non-pregnant women ($p > 0.05$) (Supplementary Table 2). Additionally, serum nervonic acid levels are elevated in the second and third trimesters and decrease again in the three months postpartum ($p < 0.05$) (Supplementary Table 2). The MUFA serum profile is similar to that of oleic acid, due to its high concentration, when compared with other fatty acids of the group (Supplementary Table 2, Supplementary Figure 4F).

Regarding the PUFA, serum levels are similar among women in the first trimester and at three months postpartum ($p > 0.05$) (Figure 3A and 3B Supplementary Table 2). In the PUFA group, a common serum profile is observed with α -linolenic, eicosadienoic, DHGLA, Arachidonic acid (ARA) and docosahexaenoic acid (DHA). Furthermore, a gradual rise in serum levels of these acids is observed throughout gestation, being higher in the third trimester. In the three months postpartum, serum levels are significantly decreased ($p < 0.05$) (Supplementary Table 2). On the other hand, the serum profiles of linoleic, γ -linolenic, eicosapentaenoic and docosadienoic acids have some common characteristics. In this group of PUFA, serum levels decrease in the first trimester when compared with the other groups ($p < 0.05$) (Supplementary Table 2). Docosadienoic acid is not detected in the first trimester and then significantly rises in the second and third trimesters, when compared with the non-pregnant group ($p < 0.05$) (Supplementary Table 2). In the PUFA group, serum levels in men are lower when compared with those of non-pregnant women ($p < 0.05$) (Figure 3). Overall, the PUFA serum profile is similar to linoleic acid because of its high serum concentration when compared with the other members of the group.

Regarding TFA serum levels, these fatty acids are elevated in non-pregnant women when compared with men ($p < 0.05$) (Figure 4A and 4B; Supplementary Table 2). Serum levels of TFA rise during the second and third trimesters ($p < 0.05$) (Figure 4A and 4B; Supplementary Table 2). No differences in serum levels of TFA are observed among non-pregnant women, first trimester women and at three months postpartum ($p > 0.05$). In addition, elaidic acid serum levels decrease in the first trimester when compared with non-pregnant women, and then increase in the third trimester ($p < 0.05$) (Supplementary Table 2). Linoleic acid levels are elevated since the first trimester and are higher towards the end of pregnancy and then decrease three months postpartum ($p < 0.05$) (Supplementary Table 2). Serum levels of C18:3 (ω -3) are increased during the third trimester and then decrease three months postpartum ($p < 0.05$) (Supplementary Table 2).

Omega-3 fatty acid serum levels are similar among non-pregnant women and women in first trimester ($p > 0.05$) (Supplementary Table 2, Supplementary Figure 1A and 1B). In addition, serum levels of omega-3 fatty acids rise from the second trimester ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 1A and 1B). Omega-3 fatty acid serum levels at three months postpartum decrease, being similar to those of women in first trimester and non-pregnant women ($p > 0.05$) (Supplementary Table 2, Supplementary Figure 1A and 1B).

Omega-6 fatty acid serum levels in men are lower compared to non-pregnant and pregnant women ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 2A and 2B). Serum levels of omega-6 fatty acids rise in the second trimester, with the highest levels at the end of gestation ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 2A and 2B). Omega-6 fatty acid serum levels are similar among non-pregnant women, women in the first – trimester and at three months postpartum. The serum profile of this group is similar to that of linoleic acid, owing to its high concentration in comparison to the other members.

The results show that total fatty acid serum levels are significantly elevated in non-pregnant women compared to men ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 3A and 3B). Total fatty acid serum levels rise from the second trimester, reaching peak levels at the end of gestation ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 3A and 3B). Serum levels of total fatty acids decrease three months postpartum when

compared to first trimester and non-pregnant women ($p < 0.05$) (Supplementary Table 2, Supplementary Figure 3A and 3B). Finally, in Supplementary Figure 3B, the percentage distribution of SFA, MUFA, PUFA, TFA and other fatty acids can be observed.

Discussion

This study demonstrates the serum profiles of different essential and non-essential fatty acids throughout pregnancy. This prospective cohort study of pregnant women, during the three trimesters of pregnancy and three months postpartum, shows the changes of serum concentration of total fatty acids, SFA, MUFA, PUFA, TFA, omega-3 and omega-6 fatty acids families. Additionally, serum levels of fatty acids across pregnancy are compared against serum concentrations in healthy non-pregnant women and a group of healthy men. These serum profile changes of different fatty acid families during gestation are caused by metabolic adaptations throughout pregnancy, related to the anabolic or catabolic phases of pregnancy and the uptake of fatty acids by the fetoplacental unit.

During gestation, the sole source of fetal nutrients is the mother. Her intake of saturated or unsaturated fatty acids plays important roles during fetal development and growth. In the study developed by Al et al., plasma levels of total fatty acids were elevated between weeks 10 and 40 of gestation, more pronounced between weeks 10 and 30 and less pronounced after week 30 until the end of gestation [7]. Also, Al et al. [7] showed that at 6 months postpartum maternal total fatty acid serum levels decreased, becoming similar to levels at 10 weeks of gestation. The present study observed serum levels of maternal total fatty acids are higher from the second trimester until the end of the pregnancy compared to non-pregnant women serum levels. These serum levels decrease at three months postpartum (Supplementary Figure 3A).

In this study, SFA was observed to contribute to the highest percentage to total serum fatty acids during gestation, followed by PUFA and MUFA (Supplementary Figure 3B). On the other hand, the percentages in serum levels of SFA and PUFA are relatively similar in men, non-pregnant, and postpartum women (Supplementary Figure 3B). It is important to note that the percentages of serum MUFA are the same in total fatty acids in the different groups studied.

In the longitudinal study by Lindsay et al., liquid chromatography (LC) with mass spectrometry (MS) was

utilized to study plasma levels between weeks 13.1 ± 1.8 , 20.5 ± 1.4 and 30.5 ± 1.4 of gestation [8]. It was demonstrated that the plasma levels of SFA do not change during the three gestational periods studied [8]. Contrary to this, the present study shows that the concentration of the SFA family increases significantly from the first trimester, being higher in the third trimester (Figure 1A). Lindsay et al. and the present study found that palmitic acid has the highest serum levels of SFA family, followed by stearic acid (Figure 1B). The data from both studies evidence that SFA serum levels are significantly increased from week 10 of gestation until delivery [7],[8]. Changes in percentages of palmitic acid are very significant during the second and third trimesters ($p < 0.05$). However, Lindsay et al. did not find changes in these percentages [8]. There are studies suggesting that SFA may have adverse effects on glucose metabolism and insulin resistance [9]. Vidakovic et al. observed that overweight and obese pregnant women have higher plasma SFA levels when compared to normal weight women [10]. They also observed an increase in serum concentrations of palmitic and stearic acid [10]. Those results correlate with the present study, where palmitic acid rises from the second trimester in healthy pregnant women with a normal weight.

Oleic acid is considered the most common MUFA in the diet, followed by palmitoleic acid [11]. In the present study, oleic acid had the highest concentration within the MUFA group during gestation followed by palmitoleic acid (Figure 2B). The percentage of oleic acid does not vary during gestation, whereas the percentage of palmitoleic acid increases in the second and third trimesters (Figure 2B). Vidakovic et al. demonstrated a positive correlation between weight gain and palmitoleic acid serum levels [10]. In the present study, an increase in the percentage of palmitoleic acid in the second and third trimesters was observed in concordance with this previous study [10]. Al et al. showed that MUFA are elevated throughout gestation and are reduced 6 months postpartum, similar to the present study. In contrast, Lindsay et al. analyzed 5 members of MUFAs, in which there were no variations during gestation, and oleic acid, had the highest concentration in the group [8].

The Omega-6 and Omega-3 series of the PUFA family are precursors of molecules related to cellular signaling and the structure and function of the phospholipid bilayers in cellular membranes [12]. The present study reported that linoleic acid has the highest serum levels in the PUFA group, whereas ARA represents the second

Table 1: Characteristics of the subjects.

Variable	Men	Healthy non-pregnant women	Healthy pregnancy (n=100)			3 months post-partum (n=100)	p-value*
	(n=48)	(n=50)	Early pregnancy	Middle pregnancy	Late pregnancy		
Age, years	20,27 (± 3,15)	19,96 (± 2,57)	24,37 (±6,56)	24,37 (±6,56)	24,37 (±6,56)	24,37 (±6,56)	1
Height, meters	1,6 (1,56-1,64)	1,59 (1,57-1,63)	1,58 (± 0,06)	1,58 (± 0,06)	1,58 (± 0,06)	1,58 (± 0,06)	1
Weight, kg	56,5 (53,38-63,25)	55 (51-59,5)	56,63 (± 8,95)	61,53 (± 9,25)	64,72 (± 10,23)	58,15 (± 9,16)	0
BMI, kg/m2	22,21 (21,03-23,73)	21,51 (19,96-23,54)	22,81 (± 2,94)	24,45 (22,58-26,6)	25,9 (23,48-28,02)	23,12 (21,02-25,48)	0
Fasting glucose, mg/dL	84 (78-88,48)	84 (80-88,92)	78 (73-82)	75,01 (± 7,74)	74 (69-78)	79 (75-84)	0
Fasting insulin, µUI/mL	9,25 (4,73-12,35)	9,45 (± 5,04)	9,5 (6,53 – 11,48)	11,55 (± 5,11)	13,62 (± 5,85)	10,5 (± 6,72)	0,061
HOMA-IR	1,88 (1,01-2,62)	1,92 (1,07-2,67)	1,76 (1,23–2,28)	2,17 (± 1,05)	2,51 (± 1,22)	2,09 (± 1,4)	0,428
Total cholesterol, mg/dL	159,2 (142,6-181,1)	157,2 (145-171,5)	166,15 (± 29,96)	218 (193,8-252)	231,5 (200,2-256,5)	176,2 (± 37,5)	0
HDL-cholesterol, mg/dL	48,98 (44,76-56,26)	50,8 (46,48-57,97)	58,67 (± 11,32)	69,56 (62,9-79,16)	67,06 (59-77)	53,33 (± 9,92)	0
LDL-cholesterol, mg/dL	115,1 (90,96-133,7)	107,9 (± 29,26)	98,69 (79,95-123)	117 (92,75-52,2)	125,6 (± 42,33)	103,1 (± 30,51)	0
VLDL-cholesterol, mg/dL	17,22 (± 6,52)	16,36 (12,53-19,24)	23,53 (± 9,24)	39,47 (± 14,37)	49,66 (± 17,78)	19,34 (± 10,32)	0
Triglycerides, mg/dL	86,01 (± 32,9)	83,8 (63,5-96,2)	117,81 (± 46,34)	198,03 (± 71,98)	249,56 (± 89,81)	96,75 (± 51,94)	0
Protein C reactive, mg/L	1,65 (±1,44)	2,01 (± 2,3)	5,13 (± 2,84)	5,23 (± 2,89)	6,41 (± 3,44)	2 (1,1–3,6)	0

*p-value: differences between the three periods of pregnancy (early, middle and late). A p-value < 0,05 was considered statistically significant. Non-normally distributed data are listed as median (IQR). Normally distributed data are listed as mean ± SD.

group in prevalence (Figure 3A). Total fatty acids in the PUFA family rise during gestation (Figure 3A). In addition, the concentrations of the members of this group do not change during the gestation (Figure 3B). Similarly, Lindsay et al. demonstrated that the highest levels of fatty acids in the PUFA family are linoleic, ARA, DHA and EPA [8]. They observed that the plasma levels of some members of this family decrease along gestation [8]. Al et al. demonstrated that plasma levels of linoleic and DHA did not change throughout gestation, while ARA decreased [7].

Trans-fatty acids cannot be synthesized in the human body, therefore diet is the sole source of these acids [13]. In the present study, the two main members of the TFA

family during gestation are elaidic acid and linolelaidic acid (Figure 4B). In addition, an increase of TFA was determined in the second and third trimesters (Figure 4A). Of note, there was an increase in linolelaidic acid within the TFA family during gestation, when compared to serum levels in non-pregnant and postpartum women (Figure 4B). This increase in TFA levels during pregnancy correlates with that described by Elias et al., where the majority of pregnant women consumed fast foods [14]. The percentage of elaidic acid in men is higher when compared to the other groups (Figure 4B). Thus, elevation in serum TFA concentration reflects the quality of the maternal diet, largely associated with fast foods or high-fat dairy intake [15]. Dirix et al. observed the relative

content (% w/w) of C18:1 trans-fatty acid in maternal plasma sampled during early, middle and late pregnancy, and directly after delivery [16]. These results, unlike the present study, do not show differences between the first and second trimesters, and there is a decrease in the percentage of trans-fatty acid in the third trimester and in the immediate postpartum [16]. A similar pattern to this was observed at three months postpartum (Figure 4A). Therefore, due to this change between gestation and the postpartum period, and despite the lack of data on dietary intake of the study group, it can be inferred that changes in the physiology of gestation could influence the concentration of fatty acids in blood, although its main source is known to be exogenous. As previously mentioned, in addition to dietary factors, other aspects also contribute to the individual fatty acid distribution (oxidation, conversion, incorporation) [15].

Regarding the PUFA of the Omega-3 series, it is important to highlight the increase in the percentage of DHA levels in pregnant women when compared to non-pregnant and postpartum women. The percentages in ALA levels relative to the other members of the family do not change throughout gestation (Supplementary Figure 1A). In the omega-6 series, it is important to note that linoleic acid, followed by ARA, represents the highest percentages of the series (Supplementary Figure 2B). The behavior of DHA and ARA, as presented in Supplementary table 2, is similar to that reported by Al et al., in which they showed an increase of these two fatty acids along gestation and a decrease six months postpartum [17]. These authors also report a 52% increase in DHA during gestation [17], a percentage similar to the present study (Supplementary Table 2, Supplementary Figure 1B). This increase might be secondary to the enzyme activity involved in DHA synthesis from its precursors or due to the mobilization of maternal fat reserves at the end of gestation [17].

Conclusions

In conclusion, this study shows significant differences in the lipid profiles among pregnant women and healthy non-pregnant women and men, with a decrease in the serum profile of all fatty acid families observed in the postpartum period. Thus, the changes in the serum profiles of the lipids studied during pregnancy could be explained by the anabolic and catabolic adaptations mediated by hormonal changes in normal conditions.

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