Clinical Nutrition xxx (2017) 1–9

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Plasma fatty acid patterns during pregnancy and child's growth, body composition, and cardiometabolic health: The Generation R Study

Trudy Voortman [a, b, *], Myrte J. Tielemans [a, b], Wendy Stroobant [a], Josje D. Schoufour [a], Jessica C. Kiefte-de Jong [a, c, d], Jolien Steenweg-de Graaff [a], Edith H. van den Hooven [a], Henning Tiemeier [a, e], Vincent W.V. Jaddoe [a, b, c], Oscar H. Franco [a]

[a] Department of Epidemiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[b] The Generation R Study Group, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[c] Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
[d] Leiden University College, The Hague, The Netherlands
[e] Department of Child and Adolescent Psychiatry/Psychology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 21 November 2016
Accepted 7 April 2017

Keywords:
Fatty acids
Pregnancy
Children
Obesity
Cardiometabolic health
Cohort

SUMMARY

Background: Exposure to different concentrations of fatty acids during fetal life may affect growth and metabolism. However, most studies examined individual fatty acids, whereas concentrations highly correlate and may interact with each other. We aimed to evaluate patterns of plasma fatty acids during pregnancy and their associations with growth, body composition, and cardiometabolic health of the 6-year-old offspring.

Methods: This study was performed in 4830 mother–child pairs participating in a population-based cohort in the Netherlands. Around 20 weeks of gestation, we measured plasma phospholipid concentrations of 22 fatty acids, in which we identified three fatty acid patterns using principal component analysis: a '*high n-6 polyunsaturated fatty acid (PUFA)*' pattern, a '*monounsaturated and saturated fatty acid (MUFA and SFA)*' pattern, and a '*high n-3 PUFA*' pattern. When the children were 6 years old, we measured their anthropometrics and detailed body composition (using dual-energy X-ray absorptiometry), and we calculated their body mass index (BMI), fat mass index (FMI), fat-free mass index (FFMI). At the same age, children's blood pressure, and serum insulin, HDL-cholesterol, and triacylglycerol were measured.

Results: After adjustment for confounders and the other patterns, a higher score for the '*high n-6 PUFA*' pattern during pregnancy was associated with a higher height, BMI, and FFMI in the offspring at 6 years, but not independently with cardiometabolic outcomes. The '*MUFA and SFA*' pattern was not consistently associated with child body composition or cardiometabolic health. A higher score for the '*high n-3 PUFA*' pattern was associated with a lower FMI, higher FFMI, higher HDL-cholesterol, and lower triacylglycerol.

Conclusions: Our results suggest that plasma fatty acid patterns during pregnancy may affect offspring's body composition and cardiometabolic health. Specifically, a pattern characterized by high *n*-3 PUFA levels was associated with a more favorable body composition and blood lipid profile.

1. Introduction

Specific nutritional exposures in critical periods in fetal life may have a lasting influence on subsequent growth and cardiometabolic health [1,2]. Fatty acids have received considerable interest in this context because of their diverse roles in for example cell membrane synthesis, inflammatory processes, and gene expression [3]. During pregnancy, fatty acids may affect placental function [4] and fatty acids are transferred from the

Abbreviations: ARA, arachidonic acid; BF%, body fat percentage; BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; DGLA, dihomo-γ-linolenic acid; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; DXA, dual-energy X-ray absorptiometry; EPA, eicosapentaenoic acid; FFMI, fat-free mass index; FFQ, food-frequency questionnaire; FMI, fat mass index; HDL-C, high-density lipoprotein cholesterol; MUFA, monounsaturated fatty acid; LA, linoleic acid; LDL-C, low-density lipoprotein cholesterol; PCA, principal component analysis; PUFA, polyunsaturated fatty acid; SBP, systolic blood pressure; SDS, standard deviation score; SFA, saturated fatty acid; TAG, triacylglycerol.

* Corresponding author. Department of Epidemiology, Erasmus MC, Office Na-2903, PO Box 2040, 3000 CA Rotterdam, The Netherlands.
E-mail address: trudy.voortman@erasmusmc.nl (T. Voortman).

http://dx.doi.org/10.1016/j.clnu.2017.04.006
0261-5614/

mother to the fetus [5]. Differences in fatty acid concentrations may thereby persistently affect growth and metabolism of the child from early life onwards [6–8].

Previous research in this area mainly focused on polyunsaturated fatty acids (PUFAs). Although a few studies, including previous analyses in our study, suggest favorable effects of omega-3 (*n*-3) PUFAs in early life on later body composition and insulin levels [5,9–11], overall evidence for PUFAs in relation to subsequent cardiometabolic health remains inconclusive [12]. Studies on saturated (SFA) or monounsaturated fatty acid (MUFA) levels in early life in relation to later cardiometabolic health in humans are scarce. Furthermore, most previous studies only targeted a few selected individual fatty acids (e.g., DHA and EPA) or groups of fatty acids (e.g., total *n*-3 PUFAs), whereas there are numerous circulating fatty acids of which the concentrations highly correlate [13]. By only examining individual fatty acids, synergistic or additive effects may be missed [14]. An approach that can overcome this limitation because it takes these interrelations into account, is to study patterns of fatty acids, which can be identified with for example principal component analysis (PCA) or other data reduction techniques. These analyses can be used to identify novel patterns in complex data. A few studies have applied this approach to fatty acids and identified various patterns, for example patterns characterized by high concentrations of n-3 PUFAs, or by very long-chain fatty acids. These studies have also shown associations of different types of circulating or adipose tissue fatty acid patterns with weight changes [15], metabolic syndrome [16], arterial stiffness [17], insulin resistance [14], and coronary atherosclerosis [13]. However, whether patterns of fatty acids during pregnancy may affect health of the offspring has not been studied. We aimed to identify patterns of plasma phospholipid fatty acid among women during pregnancy and to study whether these patterns are associated with detailed measures of growth, body composition, and cardiometabolic health of their children in a large cohort of 4830 mother–child pairs.

2. Methods

2.1. Study population

This study was embedded in the Generation R Study, a population-based prospective cohort in Rotterdam, the Netherlands [18]. All participants provided written informed consent. A total of 8663 women were enrolled before 25 weeks of gestation. For 6999 of these women we had complete information on plasma fatty acid status. Of this group, 6925 women gave birth to singleton live-born children, of whom 4890 visited our research center around the age of 6 years for body composition and cardiometabolic health measurements (Fig. 1).

2.2. Maternal plasma fatty acid patterns

Non-fasting venous blood samples were collected in mid-pregnancy at a median gestational age of 20.5 weeks (95% range 16.5–24.9) and transported and stored as described previously [19]. For the fatty acid analyses, plasma samples were transported to the Division of Metabolic Diseases and Nutritional Medicine, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University of Munich, Germany. The fatty acid composition of plasma phosphoglycerides was analyzed using gas chromatography [20]. The average coefficient of variation was 15.7% [21].

We expressed the concentrations of all 22 individual fatty acids for which we had information available in weight percentage (wt%) of total fatty acids in the chromatogram (Table 1). We performed a PCA on the wt% of these 22 fatty acids among all women in our study with information on fatty acid profiles (n = 6999). PCA is a statistical data reduction technique that groups individual variables (e.g., the individual fatty acids) into groups, called principal components (e.g., fatty acid patterns), that explain the largest possible variation in the original variables. Based on the scree-plot obtained from the PCA, an Eigenvalue ≥2, and the distinctive character of the principal components, we selected the first three principal components, or fatty acids patterns, for subsequent analyses. A *Varimax* rotation was used to improve the interpretability of the patterns. Factor loadings, which describe how strongly each individual fatty acid contributes to each fatty acid pattern, were calculated and are presented in Table 1. On the basis of high factor loadings (≥|0.20|) for the respective fatty acids (Table 1), we named these patterns: 1) '*high n-6 PUFA*' pattern; 2) '*MUFA and SFA*' pattern; and 3) '*high n-3 PUFA*' pattern. Each woman had an individual score on each of the fatty acid patterns.

2.3. Child body composition and cardiometabolic outcomes

Children's height and weight up to the age of 4 years were measured during routine visits to Child Health Centers at median (95% range) ages of 1 (1,2), 2 (2,3), 3 (3,4), 4 (4,5), 6 (5–8), 11 (10–13), 14 (13–16), 19 (17–21), 24 (23–28), 30 (29–34), 36 (35–40), and 45 (44–48) months. At their median age of 5.9 years (95% range 5.6–6.6), we measured the children's height, weight, body composition, and cardiometabolic health factors in our dedicated research center at Erasmus University Medical Center [18]. Height was determined with a Harpenden stadiometer (Holtain Limited, Dyfed, U.K.), and weight was measured using a mechanical personal scale (SECA, Almere, the Netherlands). Total and regional (including android and gynoid) body fat and fat-free mass were measured with a dual-energy X-ray absorptiometry (DXA) scanner (iDXA, GE-Lunar, 2008, Madison, WI, USA), using enCORE software v.13.6. As primary body composition outcomes, we calculated body mass index (BMI) (weight (kg)/height $(m)^2$), fat mass index (FMI) (fat mass (kg)/height $(m)^2$), and fat-free mass index (FFMI) (fat-free mass (kg)/height $(m)^2$) [22,23]. We additionally calculated body fat percentage (BF%) by expressing total fat mass as percentage of total body weight and the ratio of android fat mass divided by gynoid fat mass. We defined child's weight status as underweight, normal weight, or overweight on the basis of the Cole criteria (2000).

Children's non-fasting blood samples were obtained, in which we measured concentrations of insulin, C-peptide, triacylglycerol (TAG), and total, low-density lipoprotein (LDL-C), and high density lipoprotein cholesterol (HDL-C) with enzymatic methods (Cobas 8000, Roche, Almere, the Netherlands) [19]. While the children were lying, systolic (SBP) and diastolic blood pressure (DBP) were measured at the right brachial artery for four times with one-minute intervals (Accutorr Plus™, Paramus, NJ, USA). For our analyses, we used mean SBP and mean DBP of the last three measurements.

To account for age and sex-related differences and to enable comparison of effect estimates across the different outcomes, we calculated age- and sex-specific SD scores (SDS) for all outcomes. As no reference data is available for this age group, these SDSD were calculated on the basis of the total Generation R Study population with cardiometabolic data at 6 years (n ranging from 4414 to 6491) [18].

In line with previous studies that defined scores for a metabolic syndrome-like phenotype in children [24], we created a continuous score including five components: BF%, blood pressure, HDL-C, TAG, and insulin concentrations. The cardiometabolic risk factor score

Please cite this article in press as: Voortman T, et al., Plasma fatty acid patterns during pregnancy and child's growth, body composition, and cardiometabolic health: The Generation R Study, Clinical Nutrition (2017), http://dx.doi.org/10.1016/j.clnu.2017.04.006