

Use of Plastic Packages for Food and Liquids in a prospective cohort of pregnant patients – Association analyses with birthweight and pregnancy duration

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Abstract

Purpose: Exposure to endocrine disrupting chemicals (EDCs) is ubiquitous in modern civilization and their impact on hormonal regulation in vivid organisms is well established. These substances also seem to play a pivotal role during pregnancy as they might influence birth and pregnancy outcomes, such as fetal birthweight and pregnancy duration.

The objective of this study is to investigate the associations of increased EDC exposure during pregnancy with changes of fetal birthweight and pregnancy duration.

Methods: Individual use of plastic food and liquid packages was evaluated in 493 pregnant patients from the Clinical Gravidity Association Trial and Evaluation (CGATE) cohort using a three item lifestyle questionnaire concerning plastic consumption habits. To assess exposure to EDCs patients were further grouped into risk categories, and the associations with birthweight and pregnancy duration were investigated using a linear regression model.

Results: For none of the investigated plastic consumption habits concerning drinking water, food from cans/plastic or beverage cartons (Tetra Pak) a statistically significant association with birthweight could be found. Moreover, no significant correlation between plastic consumption in regards of drinking water and food from cans/plastic with pregnancy duration could be detected. Interestingly, a statistically significant pregnancy prolongation of 0.4 weeks ($p = 0.01$, 95% CI: 0.1; 0.7) was observed with increasing consumption of Tetra Pak.

Conclusion: The impact of plastic package consumption during pregnancy does not seem to have a major effect on birthweight or pregnancy duration, however the direction in which the statistically non-significant differences were seen were into the expected direction. Therefore larger studies are warranted to investigate this potentially important epidemiological factor.

Introduction

According to the World Health Organization (WHO), a total of about 800 exogenous substances or mixtures - referred as endocrine disrupting chemicals (EDCs) - are known (1). For example, phthalates are found as plasticizers in various plastic packaging materials and are not chemically bound to plastics or other products. Consequently, these substances can easily detach themselves and hence migrate into food or even water and enter human organisms via daily food and fluid intake (2). During pregnancy EDCs are able to pass over to the fetus through the placental barrier and postpartum via breast milk directly to the child (3).

EDCs are capable of interfering with the hormone system of living organisms. However, the exact pathophysiological mechanisms of these substances are still unknown (1).

EDCs are able to interact with estrogen- and/or androgen receptors, thus leading to disruption or modulation of normal estrogen- and/or androgen-ligand-activity (4, 5). Moreover, they are known to

increase intracellular peroxisome proliferator-activated receptors, and thereby cause deactivation of 17 β -hydroxysteroid-dehydrogenase (converting enzyme of androstenedione into testosterone and estrone into estradiol). This cascade is known to be associated with preterm birth (PTB) (6-8).

Fetal birthweight might also be affected through hormonal imbalance caused by the interaction of EDCs with estrogen receptors or through alteration of lipid levels (9, 10).

Pregnancy duration was also observed to be impacted by various hormonal effects of EDCs, such as bisphenol A (BPA). As “synthetic hormone” BPA is able to bind to estrogen receptors leading to estrogen-mediated gene expression (11). Moreover, this substance class was found to alter the signal cascade of thyroid synthesis and to have an affinity to glucocorticoid receptors (12). Thus, the inflammatory potential of BPA, which is reflected by increase of C-reactive-protein might be responsible for reduction of pregnancy duration (13).

Summarizing current evidence regarding EDC exposure of pregnant patients and their offspring and the potential impact on pregnancy and birth outcomes, such as birthweight and pregnancy duration, a heterogeneous data situation is obvious. The objective of this work was to further investigate the associations between increased exposure to EDCs during pregnancy and primary outcome parameters changes in birthweight and pregnancy duration. As modern plastic packaging materials for foods and drinks contain considerable amounts of EDCs, individual plastic consumption was assessed with a pregnancy diary including dietary patterns of patients from the Franconian “Clinical Gravidity Association Trial and Evaluation (CGATE)” cohort and further correlated with birthweight in 490 and pregnancy duration in 493 patients.

Methods

Within the scope of the CGATE program - a prospective observational study in pregnant patients from March 2010 until December 2014 - a total of 688 individuals were recruited with the aim of identifying novel biomarkers to predict unfavorable events during pregnancy and adverse birth outcomes. Inclusion criteria were patients with sonographically viable and intrauterine singleton gravidity before 14 + 0 weeks of gestation, patient age of at least 18 years and willingness to complete a pregnancy diary, a structured questionnaire concerning lifestyle, body weight, nutrition and pregnancy-related disorders, such as restless leg syndrome and depression, which had to be completed every month until the end of pregnancy. Moreover biomarkers (14, 15), blood and urine samples were collected during study inclusion, optional visits between 20 – 23 weeks’ gestation and at delivery. Exclusion criteria were patients with multiple pregnancies, patients experiencing miscarriage/fetal demise or being diagnosed with fetal anomalies, individuals with missing consent-forms and/or insufficient pregnancy diary documentation. Moreover, the maternity record (Mutterpass) - a mandatory document for obstetricians to monitor pregnancy in Germany – and the patient’s chart at birth were obtained for documentation of mother-, child- and pregnancy-characteristics. Patients were followed up until 6 months postpartum. A total of 493

individuals met the study criteria. From all of those pregnancy duration and from 490 subjects birthweight values were available and further included into statistical analyses.

Individual plastic consumption was evaluated using a three item lifestyle questionnaire (see **Table 1**) within the pregnancy diary. Patients were asked to complete the diary/questions at study begin (first trimester), 16, 20, 24, 28, 32, 36 and 38-40 weeks of gestation.

Plastic consumption during pregnancy was categorized into “*Drinking Water from Plastic Packaging*”, “*Food from Plastic Packaging and Cans*” and “*Drinks from Beverage Cartons (Tetra Pak)*”. In order to be able to statistically present and investigate the following described answer possibilities of the three questions concerning exposition to EDCs, these were grouped into consumption habits and following exposure risk categories: 0 (low risk), 1 (moderate risk) and 2 (high risk) (see **Table 1**).

To assess the patient’s habits concerning drinking water consumption answer possibilities of question 1 “*From which source do you directly consume drinking water?*” were categorized as following: Answers a) “*Mostly glass bottles*” and b) “*Mostly tap water*” as category 0: “*No plastic use*”; answer c) “*Don’t know exactly (mixed)*” as category 1: “*Moderate plastic use*”; answers d) “*Mostly reuseable plastic bottles*”, e) “*Mostly disposable plastic bottles*” and f) “*I don’t drink water, only other drinks*” as category 2: “*Predominantly plastic use*” (see **Table 1**).

Table 1 Three item lifestyle questionnaire within the pregnancy diary of the CGATE-cohort patients

| Individual Plastic Consumption | Consumption Habit | Category |
|---|---------------------------|-----------------|
| <i>“Drinking Water from Plastic Packaging”</i> | | |
| Q1 From which source do you directly consume drinking water? | | |
| a) Mostly glass bottles | No plastic use | 0 |
| b) Mostly tap water | No plastic use | 0 |
| c) Don't know exactly (mixed) | Moderate plastic use | 1 |
| d) Mostly reusable plastic bottles | Predominantly plastic use | 2 |
| e) Mostly disposable plastic bottles | Predominantly plastic use | 2 |
| f) I don't drink water, only other drinks | Predominantly plastic use | 2 |
| <i>“Food from Plastic Packaging and Cans”</i> | | |
| Q2 How often do you consume food or ready meals from cans or plastic packaging? | | |
| a) Never | (almost) never | 0 |
| b) 1-2 times per month | (almost) never | 0 |
| c) 1-2 times per week | 1-2/week | 1 |
| d) Almost daily/daily | (almost) daily | 2 |
| <i>“Drinks from Beverage Cartons (Tetra Pak)?”</i> | | |
| Q3 How often do you consume drinks (including milk) from beverage cartons (Tetra Pak)? | | |
| a) Never | (almost) never | 0 |
| b) 1-2 times per month | (almost) never | 0 |
| c) 1-2 times per week | 1-2/week | 1 |
| d) Almost daily/daily | (almost) daily | 2 |
| <i>Answer possibilities categorized into consumption habits and exposure risk categories 0: low risk, 1: moderate risk and 2: high risk</i> | | |

For evaluation of food consumption from plastic packaging and cans answer possibilities of question 2 “How often do you consume food or ready meals from cans or plastic packaging?” were categorized as following: Answers a) “Never” and b) “1-2 times per month” as category 0: “(almost) never”; answer c) “1-2 times per week” as category 1: “1-2/week”; answer d) “Almost daily/daily” as category 2: “(almost) daily” (see **Table 1**).

Question 3 “How often do you consume drinks (including milk) from beverage cartons (Tetra Pak)?” was answered and categorized in analogy to question 2 (see **Table 1**).

Mean values of categorized answer possibilities – ranging from 0 to 2 - were only calculated if the questionnaire on nutrition and lifestyle was completed at least at three time points during pregnancy period.

Birthweight was measured after parturition in the delivery room by the attending midwife with a standard baby scale and was subsequently entered into the birth documentation system ViewPoint 5 (© 1995-2020 General Electric Company, GE Healthcare). Birthweights of patients delivering at another hospital were obtained from the maternity record. From a total of 490 patients birthweight was documented. *Pregnancy Duration* was also documented in analogy or rather taken from the maternity record. Gestational age was calculated from the first day of the patient’s last menstrual period or corrected after fetal crown-rump-length in the first trimester, when gestational age determined by sonographic measurement was deviating more than a week. This variable was documented in all 493 individuals.

For the representation of the patient collective descriptive statistics were conducted, and the absolute use of plastic packaging during pregnancy was analyzed. Additionally, birthweight was descriptively compared with average plastic consumption per patient during pregnancy.

The associations between increased plastic consumption with changes in birthweight and pregnancy duration were analyzed using a linear regression model. The following predictors were included: child’s sex, mother’s BMI, father’s BMI, parity (> 0 versus 0) and previous miscarriages (> 0 versus 0). Plastic consumption was integrated as a continuous variable – ranging from 0 to 2 (definition see above and **Table 1**) - into the linear model.

The significance level was set to $\alpha = 0.05$. Statistical analyses were performed using the software R (Version 3.4.0, R Core Team, Vienna, Austria, 2017).

Results

A total of 490 patients were included into statistical analyses for birthweight and 493 individuals for pregnancy duration. An overview of the variables observed and the patient characteristics are shown in **Table 2**.

Table 2 Characteristics of study population

| Characteristics | mean (range) | SD |
|------------------------------------|-------------------------|----------|
| Birthweight (in kg) | 3339.6 (890.0 – 5130.0) | 519.9 |
| Pregnancy Duration (in weeks) | 39.7 (27.0 – 43.0) | 1.8 |
| BMI mother (in kg/m ²) | 23.5 (16.2 – 46.0) | 4.5 |
| BMI father (in kg/m ²) | 25.9 (17.2 – 38.9) | 3.3 |
| | n | % |
| Para | | |
| 0 | 242 | 49.3 |
| > 0 | 249 | 50.7 |
| Fetal Sex | | |
| Male | 241 | 49.2 |
| Female | 249 | 50.8 |
| Miscarriage | | |
| 0 | 361 | 73.5 |
| > 0 | 130 | 26.5 |

n = Number, *SD* = Standard Deviation

“Predominantly plastic use” in concerns of drinking water was much more common than “Moderate or no plastic use” (see **Table 3** and **Figure 1A**). The majority of patients “(almost) never” consumed food from plastic packaging and cans (see **Table 3** and **Figure 1B**). Controversially, “(almost) daily” use of Tetra Pak could be observed more frequently within the study population (see **Table 3** and **Figure 1C**). Interestingly, the consumption habits regarding all 3 plastic packaging modalities remained almost stable over all time points of pregnancy.

Table 3 Percentages of consumption habits regarding plastic packaging modalities for

| Exposure Risk Category | Trim 1 | 16 weeks | 20 weeks | 24 weeks | 28 weeks | 32 weeks | 36 weeks | 40 weeks |
|---|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| <i>Drinking Water from Plastic Packaging</i> | 370 patients | 475 patients | 482 patients | 481 patients | 483 patients | 467 patients | 376 patients | 420 patients |
| No plastic use | 28.4% | 30.3% | 30.7% | 31.2% | 31.3% | 32.8% | 34.3% | 30.5% |
| Moderate plastic use | 13.0% | 15.4% | 14.9% | 13.9% | 13.4% | 13.5% | 14.1% | 13.6% |
| Predominantly plastic use | 58.6% | 54.3% | 54.4% | 54.9% | 55.3% | 53.7% | 51.6% | 55.9% |
| <i>Food from Plastic Packaging and Cans</i> | 371 patients | 476 patients | 482 patients | 482 patients | 485 patients | 468 patients | 377 patients | 423 patients |
| (almost) never | 70.3% | 66.8% | 65.4% | 63.7% | 63.3% | 62.2% | 59.9% | 65.7% |
| 1-2x/week | 23.2% | 23.7% | 23.4% | 24.3% | 25.2% | 25.9% | 26.0% | 26.0% |
| (almost) daily | 6.5% | 9.5% | 11.2% | 12.0% | 11.5% | 11.9% | 14.1% | 8.3% |
| <i>Drinks from Beverage Cartons (Tetra Pak)</i> | 373 patients | 476 patients | 483 patients | 484 patients | 485 patients | 468 patients | 375 patients | 424 patients |
| (almost) never | 12.6% | 12.0% | 10.2% | 13.0% | 11.3% | 10.5% | 9.6% | 13.4% |
| 1-2x/week | 23.9% | 20.2% | 18.4% | 14.1% | 14.5% | 14.1% | 14.7% | 20.3% |
| (almost) daily | 63.5% | 67.8% | 71.4% | 72.9% | 74.2% | 75.4% | 75.7% | 66.3% |

drinks and food

Within the study cohort, neither high consumption of drinking water from plastic bottles (-17.8 g, $p = 0.48$, 95% CI: -66.9; 31.3), nor foods from cans or plastic packaging (-40.9, $p = 0.23$, 95% CI: -107.5; 25.7), nor drinks from Tetra Pak (-17.5 g, $p = 0.63$, 95% CI: -88.3; 53.3) revealed a statistical significant association with change of birthweight (see **Table 4**).

Table 4 Associations of high plastic consumption habits concerning all packaging modalities and change of birthweight

| Variable | Estimate (95% CI) | p-value |
|---|--------------------------|----------------|
| Drinking water (in g) | -17.8 (-66.9; 31.3) | 0.48 |
| Fetal sex (female) | -186.9 (-264.4; -109.3) | < 0.001 |
| BMI mother | 6.7 (-2.0; 15.5) | 0.13 |
| BMI father | 7.7 (-4.5; 20.0) | 0.22 |
| Parity \geq 1 | 102.4 (-24; 180.7) | 0.01 |
| Miscarriage \geq 1 | -41.9 (-129.1; 45.3) | 0.35 |
| Pregnancy Duration | 164.2 (142.3; 186.0) | < 0.001 |
| Cans/Plastic (in g) | -40.9 (-107.5; 25.7) | 0.23 |
| Fetal sex (female) | -185.4 (-263.0; -107.9) | < 0.001 |
| BMI mother | 7 (-1.8; 15.7) | 0.12 |
| BMI father | 6.7 (-5.4; 18.8) | 0.28 |
| Parity \geq 1 | 107 (28.9; 185.1) | 0.01 |
| Miscarriage \geq 1 | -41.9 (-129.0; 45.3) | 0.35 |
| Pregnancy Duration | 165 (143.2; 186.9) | < 0.001 |
| Tetra Pak (in g) | -17.5 (-88.3; 53.3) | 0.63 |
| Fetal sex (female) | -186.7 (-264.3; -109.1) | < 0.001 |
| BMI mother | 6.7 (-2.1; 15.4) | 0.14 |
| BMI father | 7.3 (-4.9; 19.5) | 0.24 |
| Parity >1 | 105.7 (27.5; 183.9) | 0.01 |
| Miscarriage \geq 1 | -42.1 (-129.3; 45.2) | 0.34 |
| Pregnancy Duration | 165.3 (143.3; 187.3) | < 0.001 |
| Overall plastic consumption (in g) | -66.9 (-166.6; 32.9) | 0.19 |
| Fetal sex (female) | -185.9 (-263.3; -108.4) | < 0.001 |
| BMI mother | 6.5 (-2.3; 15.2) | 0.15 |
| BMI father | 8.0 (-4.2; 20.2) | 0.20 |
| Parity \geq 1 | 104.2 (26.2; 182.1) | 0.01 |
| Miscarriage \geq 1 | -42.6 (-129.8; 44.5) | 0.34 |
| Pregnancy Duration | 165.2 (143.3; 187) | < 0.001 |

Moreover, an overall plastic consumption analysis including all three examined packaging modalities - drinking water, cans and plastic food packaging as well as Tetra Pak - could not display a statistically significant association between increasing plastic consumption and birthweight (-66.9 g, p = 0.19, 95% CI: -166.6; 32.9) (see **Table 4**).

Among all analyses, confounding factors child's sex (female), parity and pregnancy duration were the only variables reflecting statistically significant changes of birthweight (see **Table 4**).

In analogy, neither the correlation analyses of drinking water consumption from plastic packaging (-0.1 weeks, $p = 0.27$, 95% CI: -0.3; 0.1), nor food from cans or plastic packaging (0.1 weeks, $p = 0.51$, 95% CI: -0.2; 0.4), nor overall plastic consumption (0.2 weeks, $p = 0.42$, 95% CI: -0.3; 0.6) showed a statistical significant change of pregnancy duration (see **Table 5**).

Table 5 Associations of high plastic consumption habits concerning all packaging modalities and change of pregnancy duration

| Variable | Estimate (95%-CI) | p-value |
|---|-------------------|---------|
| Drinking water (in weeks) | -0.1 (-0.3; 0.1) | 0.27 |
| Fetal sex (female) | 0.2 (-0.1; 0.6) | 0.23 |
| BMI mother | 0 (-0.1; 0.0) | 0.51 |
| BMI father | 0 (0.0; 0.1) | 0.13 |
| Parity ≥ 1 | -0.2 (-0.6; 0.1) | 0.24 |
| Miscarriage ≥ 1 | -0.4 (-0.8; -0.1) | 0.03 |
| Cans/Plastic (in weeks) | 0.1 (-0.2; 0.4) | 0.51 |
| Fetal sex (female) | 0.2 (-0.1; 0.5) | 0.24 |
| BMI mother | 0 (-0.1; 0.0) | 0.53 |
| BMI father | 0 (0.0; 0.1) | 0.17 |
| Parity ≥ 1 | -0.2 (-0.5; 0.1) | 0.26 |
| Miscarriage ≥ 1 | -0.4 (-0.8; -0.1) | 0.03 |
| Tetra Pak (in weeks) | 0.4 (0.1; 0.7) | 0.01 |
| Fetal sex (female) | 0.2 (-0.1; 0.5) | 0.24 |
| BMI mother | 0 (0.0; 0.0) | 0.72 |
| BMI father | 0 (0.0; 0.1) | 0.26 |
| Parity ≥ 1 | -0.2 (-0.6; 0.1) | 0.23 |
| Miscarriage ≥ 1 | -0.4 (-0.8; 0.0) | 0.03 |
| Overall plastic consumption (in weeks) | 0.2 (-0.3; 0.6) | 0.42 |
| Fetal sex (female) | 0.2 (-0.1; 0.5) | 0.23 |
| BMI mother | 0 (0.0; 0.0) | 0.58 |
| BMI father | 0 (0.0; 0.1) | 0.21 |
| Parity ≥ 1 | -0.2 (-0.5; 0.2) | 0.28 |
| Miscarriage ≥ 1 | -0.4 (-0.8; 0.0) | 0.03 |

Interestingly, a statistically significant pregnancy prolongation of 0.4 weeks ($p = 0.01$, 95% CI: 0.1; 0.7) was observed for patients consuming drinks from Tetra Pak with a high frequency (see **Table 5**).

Moreover, confounding variable previous miscarriages (≥ 1) was statistically significant associated with decreasing pregnancy duration (see **Table 5**).

Discussion

This work investigated patient's consumption habits in regards of food and beverages from plastic packaging within the CGATE cohort, aiming on the specification of EDC exposure during pregnancy and the associations with changes of fetal birthweight and pregnancy duration.

BPA and phthalates are known for causing epigenetic modifications of fetuses and germ cells and thus might lead to negative fetal programming (16, 17). Moreover, phthalates affect thyroid metabolism and influence urine thyroxine levels. Johns et al. found an inverse correlation between 11 measurable phthalate metabolites in urine and the concentrations of fT3 and fT4, which was increasing with duration of pregnancy (2). Hypothyroidism might lead to mental retardation with potentially severe disability and spasticity of the child, but might also result in an increase of birthweight (18, 19).

The EARTH study including 346 patients examined pre-conceptual and prenatal urine samples in concerns of their bisphenol A and S concentration and observed an inverse relationship between bisphenol concentration and birthweight; high bisphenol levels in pre-conceptual urine were associated with an average weight reduction of 119 g (95% CI: -212; -27) and increased bisphenol concentrations in prenatal urine revealed a decrease of 75 g (95% CI: -153; 2) (20).

Within the ALSPAC study 447 mother-daughter dyads were investigated. Elevated maternal serum concentrations of perfluorooctanoate and perfluorohexane sulfonate were correlated with 133 g (95% CI: -237; 30) or 108 g (95% CI: -206; 10) lower birthweights of girls (10).

Controversially, a study from Spain analyzing data of 488 mother-child pairs from the INMA-Sabadell birth cohort found that with increasing urine concentrations of mono-benzyl phthalate femur length was increasing by 3.7% (95% CI: 0.75; 6.63) within 20 to 34 weeks of gestation. Additionally, birthweight among boys was 48 g (95% CI: 6; 90) higher. Interestingly an inverse correlation with birthweight of girls (-27 g, 95% CI: -79; 25, interaction $p = 0.04$) was observed (5). However, our results didn't reveal a statistical significant change of birthweights among individuals with increasing plastic consumption habits during pregnancy.

Further statistical analyses of CGATE data regarding the correlation of increasing food and beverage consumption from plastic packaging or cans with pregnancy duration did not show a significant association, besides Tetra Pak with a statistically significant pregnancy prolongation, highlighting that pregnancy duration might though had been affected by exposure to EDCs.

In German supermarkets, many dairy products, fruit juices and even drinking water are retailed in paperboard boxes referred as Tetra Pak. The inner layer of these beverage cartons is laminated with a thin plastic film (21). A Chinese study by Huang et al. including 207 patients analyzed the concentrations of 15 different phthalates in the cord blood after delivery and found, that an exposure to phthalates (except to dicyclohexyl phthalate) was statistically significant associated with a decrease of pregnancy duration and with PTB (6). Padmanabhan et al. investigated 40 patients in Michigan and found no

association between maternal EDC levels and pregnancy duration (11), which is in accordance with a study from Wolff et al. including a cohort of 367 patients from New York City (22). Within a collective of 60 individuals from Mexico City, Cantonwine et al. found, that elevated BPA urine concentrations during pregnancy had an odds ratio of 2.5 (95% CI: 1.1; 6.0) for occurrence of PTB before 37 weeks of gestation (23). Another study by Cantonwine et al. investigated 130 PTB cases and 352 term controls in Birmingham and Boston. Mother's urine was tested for BPA concentration at four time points during pregnancy and had no significant association with PTB (OR = 1.21, 95% CI: 0.79; 1.85). However, stratified analyses of sexes revealed a significant correlation of BPA with PTB in girls (OR = 1.8, p-value = 0.04, 95% CI: 1.02, 3.13) (12).

Controversially, a study from 2009 by Adibi et al. examining 300 patients in the United States found an association between phthalate concentration and longer duration of pregnancy. They observed a pregnancy prolongation by 1.1 to 1.3 days. This association was even stronger, when comparing the concentrations of phthalate metabolites in individuals at the 75th percentile and the 25th percentile (2.3 days, CI: 1.4; 3.3) (24).

Based on the CGATE data it can be stated, that there was no median "excessive" consumption of food from cans and plastic packaging, which becomes evident after statistical analysis of question 2 in the pregnancy diary, where option "*(almost) never*" was chosen most often. Thus, the overall exposure of our patient collective to EDCs might rather have been intermediate to low. Accordingly, change of fetal birthweight was not statistically significant within this study population.

Two Italian research groups investigated bisphenol concentrations of most popular beverages packed in cans, plastic containers, glass bottles and Tetra Pak in Campania province (Italy) and detected, that 100% of milk products contained BPA, whereas BPA was only found in 57% of carbonated and 50% of non-carbonated drinks. Interestingly, dairy products showed the highest BPA levels, which might be explained by precipitation of bisphenols through presence of milk lipids. Within the groups of carbonated and non-carbonated beverages cans showed highest BPA concentrations, followed by plastic packaging and Tetra Pak. Liquids from glass bottles were never contaminated with bisphenols (25-27). Consequently, beverages packed in Tetra Pak seem to have lowest EDC concentrations among all frequently used plastic packaging materials. This might be an explanation for observed pregnancy prolongation within the group of frequent Tetra Pak use in CGATE, as this subgroup regularly consumed liquids from a more "harmless" packaging source.

Limitations of this study are missing analyses of maternal urine/serum or fetal cord blood and shortage of the patient questionnaire to exactly determine EDC exposure. Strengths are the prospective cohort design, the high number of participating individuals, simplicity of the patient questionnaire, and especially the "freedom" to keep a pregnancy diary to avoid unnecessary and stressful study visits.

Conclusion

Although majority of evidence reflects, that increased exposure to EDCs, such as BPA or phthalates, is more likely to reduce birthweight and duration of pregnancy, results of many studies are conflicting. Regarding these phenotypes the results of our study are in accordance with this heterogeneous data situation. Further investigations are warranted to especially better evaluate the influence of increased EDC exposure on birth and pregnancy outcomes.

Declarations

Funding

This study was departmentally funded by the Women's Center Erlangen.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable

Ethics approval

The study was approved by the Ethics Committee of the medical faculty at Friedrich Alexander University of Erlangen-Nuremberg, Erlangen, Germany.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable

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Authors' contributions

PS is the first and corresponding author and was a major contributor in writing the manuscript and interpreting the analyzed data concerning plastic consumption habits of the CGATE cohort.

CP was an essential contributor in editing and critically reviewing the manuscript.

PG, JE, MS, ES, FF were minor contributors in writing the manuscript and essential contributors in editing and critically reviewing the manuscript.

JS and LH were major contributors for statistical analyses of used CGATE cohort data.

MR is responsible for the CGATE biorepository and was a minor contributor in writing the manuscript and essential contributor in editing and critically reviewing the manuscript.

MWB is the head of the Women's Center Erlangen and in charge of the departmental funding for this study. He was a minor contributor in writing the manuscript and an essential contributor in editing and critically reviewing the manuscript.

AT is the last author and was a major contributor in writing the manuscript and interpreting the analyzed data concerning plastic consumption habits of the CGATE cohort.

All authors read and approved the final manuscript.

Compliance with Ethical Standards

Conflict of interest

PS declares that he has no conflict of interest.

CP declares that she has no conflict of interest.

PG declares that he has no conflict of interest.

JE declares that he has no conflict of interest.

MS declares that he has no conflict of interest.

ES declares that she has no conflict of interest.

FF declares that he has no conflict of interest.

JS declares that she has no conflict of interest.

LH declares that he has no conflict of interest.

MR declares that he has no conflict of interest.

MWB declares that he has no conflict of interest.

AT declares that she has no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Figures

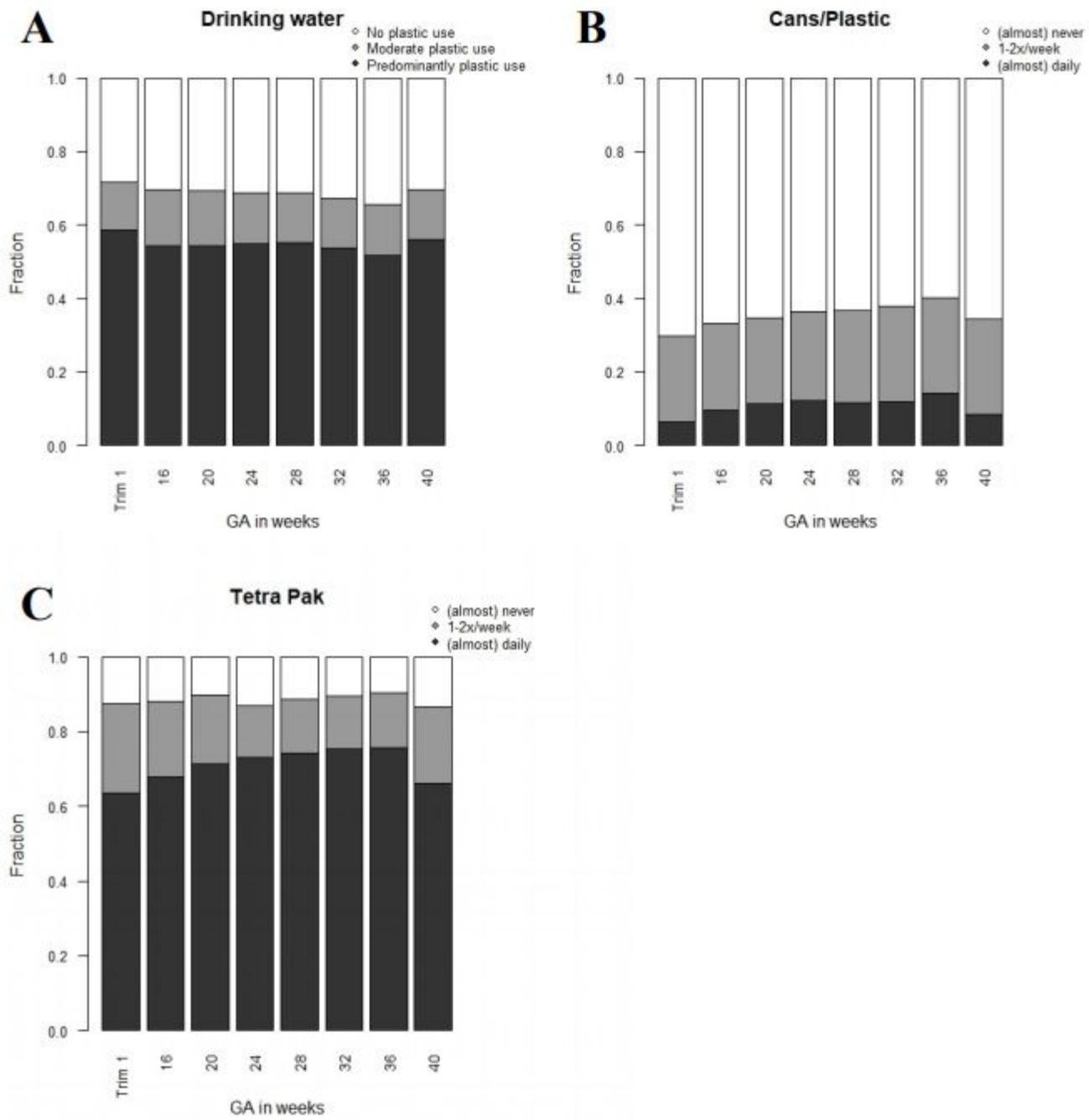


Figure 1

A-C Plastic packaging consumption habits for drinks and food within the CGATE cohort Barplots reveal consumption habits regarding plastic packaging modalities for drinks and food over all time points of the CGATE pregnancy diary questionnaire: A) Drinking water, B) Cans/Plastic, C) Tetra Pak (Trim 1 = First Trimester; GA = Gestational Age)