ASSOCIATIONS OF DIETARY INFLAMMATORY INDEX WITH BIRTH OUTCOMES AND WEIGHT STATUS AT AGE 5 AND 9: RESULTS FROM THE LIFEWAYS CROSS-GENERATION COHORT STUDY IN IRELAND

Lifeways Cross-Generation Cohort Study

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1. INTRODUCTION

Diet is an important moderator of chronic inflammation[1]. Maternal diet and chronic inflammation may influence early-life offspring health[2, 3]. No comparative data regarding parental or intergenerational associations between dietary inflammation and offspring growth exist.

2. AIM

To investigate potential associations between maternal, paternal and grandparental dietary inflammatory index (DII®) scores with offspring birth outcomes and childhood adiposity.

3. METHODS

➢ ***Participants***

1082 mother-child pairs, 333 index-child's fathers and 707 of any four grandparents.

➢ ***Dietary intake assessment***

Dietary intakes at the baseline during the 1st trimester of pregnancy were assessed using 149-item semi quantitative food frequency questionnaire (FFQ) which has been validated for use in the Irish population.

➢ ***Dietary Inflammatory index***

Energy-adjusted DII (E-DII) scores were derived from a validated FFQ for expectant mothers, fathers and up to four grandparents.

Higher DII scores represent more pro-inflammatory diets[4].

➢ ***Offspring outcomes assessment***

At birth: Low birth weight (LBW) (BW<2500g), macrosomia (BW>4000g), preterm (<36wk), post-term (>42wk).

At 5 and 9 years: weight status (overweight (BMI ≥85th pctl), obesity (BMI ≥95th pctl)).

➢ ***Covariates***

Age, height, pre-pregnancy weight, pre-pregnancy BMI, socioeconomic status, education status, alcohol intake and smoking status.

➢ ***Statistical analysis***

Kruskal Wallis test, Chi-squared test, Logistic regression analysis. Mediation analysis (process macro for *SPSS*). *SPSS* version 24.0

4. RESULTS

4.1. Characteristics of the study population

Table 1 shows the characteristics of the Lifeways participants included in this study according to parental tertiles of E-DII scores.

- Mothers and fathers with higher E-DII scores tended to be younger, separated or single, and have a lower educational level, household income and regular physical activity.
- Mothers with higher E-DII scores tended to be smokers.
- Mothers and fathers with higher E-DII scores tended to have lower dietary quality as determined by their HEI score.

Table 1. Characteristics of the study participants according to parental tertiles of E-DII scores[1]

	All participants	Tertile 1 (most anti-inflammatory)	Tertile 2	Tertile 3 (most pro-inflammatory)	p-value[2]
Maternal characteristics (n=1082)					
Maternal E-DII score	0.42±1.75	-1.51±0.87	0.41±0.45	2.35±0.90	
Maternal HEI score	52.1±8.6	57.8±7.3	51.9±7.1	46.5±7.4	**<0.001**
Age at mother recruitment (y)	30.1±5.9	32.1±5.1	30.4±5.7	27.7±6.2	**<0.001**
Pre-pregnancy BMI (Kg/m^2)	23.8±4.2	23.7±3.6	23.9±4.6	23.6±4.3	0.47
Height (cm)	163.8±6.4	164.1±6.2	163.5±6.8	163.6±6.2	0.37
Education level					**<0.001**
Below tertiary	535 (51)	135 (38)	175 (50)	225 (65)	
Tertiary or above	521 (49)	222 (62)	176 (50)	123 (35)	
Smoking during pregnancy	264 (25)	55 (16)	90 (25)	119 (33)	**<0.001**
Alcohol use during pregnancy	613 (62)	225 (67)	190 (59)	198 (61)	0.068
Marital status					**<0.001**
Married/cohabiting	830 (77)	320 (89)	284 (80)	226 (63)	
Separated/divorced/single	241 (23)	39 (11)	71 (20)	131 (37)	
Household weekly income					**<0.001**
<200£	134 (14)	26 (8)	46 (14)	62 (20)	
200-600£	490 (50)	157 (48)	166 (51)	167 (53)	
>600£	347 (36)	146 (44)	116 (35)	85 (27)	
Parity (Non-nulliparous)	584 (55)	200 (57)	207 (58)	177 (50)	0.055
Regular physical activity	182 (19)	86 (26)	49 (15)	47 (15)	**<0.001**
Paternal characteristics (n=333)					
Paternal E-DII score	1.53±1.74	-0.46±1.02	1.69±0.48	3.37±0.65	
Paternal HEI score	47.6±9.4	54.7±8.2	46.6±8.1	41.6±6.7	**<0.001**
Age at proband child birth (y)	33.6±5.5	34.9±5.8	34.0±5.1	31.9±5.1	**<0.001**
Paternal BMI (Kg/m^2)	26.6±3.9	26.6±3.4	26.9±4.4	26.3±4.1	0.54
Height (cm)	178.2±7.1	178.2±7.0	178.7±7.2	177.9±7.1	0.70
Education level					**0.046**
Below tertiary	158 (48)	45 (41)	51 (46)	62 (57)	
Tertiary or above	170 (52)	65 (59)	59 (54)	46 (43)	
Cigarette smoking	50 (22)	18 (22)	14 (18)	18 (27)	0.46
Alcohol intake	237 (77)	77 (69)	85 (81)	75 (71)	0.21
Marital status					**0.04**
Married/cohabiting	313 (96)	107 (97)	107 (98)	99 (97)	
Separated/divorced/single	14 (4)	3 (3)	2 (2)	9 (3)	
Household weekly income					**0.03**
<600£	152 (48)	43 (40)	50 (48)	59 (58)	
>600£	163 (52)	65 (60)	55 (52)	43 (42)	
Regular physical activity	134 (42)	49 (47)	53 (49)	32 (30)	**0.01**

[1] Values are means±SD for continuous variables and n (%) for categorical variables
[2] Kruskal-Wallis test for continuous variables or χ^2 test for categorical variables

Table 2. Parental nutrient intakes and E-DII scores

⬆ E-DII scores (pro-inflammatory diet)	⬇ E-DII scores (anti-inflammatory diet)
Total energy, Carbohydrate, Protein, Total Fat, MUFA, PUFA, SFA, Cholesterol	Fibre, Folate, Vitamin C, Vitamin B6, E (only in mothers)

4.2. Parental and grandparental (GP) E-DII scores and offspring outcomes

Results from the fully adjusted logistic regression models (**Table 3**) indicate that:

- Higher maternal E-DII scores were associated with increased risk of LBW (OR:1.20; 95% CI:1.02-1.47; *P*=0.03).
- Higher maternal grandmothers (MGM) E-DII scores were associated with increased risk of macrosomia (OR 1.35, 95% CI 1.02-1.79, *P*=0.03).
- Higher paternal and paternal grandmothers (PGM) E-DII scores were associated with greater risk of childhood overweight/obesity (OW/OB) at 5 years (OR: 1.03; 95% CI:1.01-1.19; *P*=0.04 and OR: 1.07; 95% CI:1.05-1.09; *P*=0.01, respectively).
- The association with the PGM E-DII persisted at age 9 (OR:1.13; 95%CI:1.01-1.90; *P*=0.04).

Table 3. Associations between parental and GP E-DII scores and binary offspring outcomes and weight status at 5 and 9 years[1]

E-DII scores	LBW	Macrosomia	Preterm birth	Post-term birth	OW 5y	OB 5y	OW/OB 5y	OW 9y	OB 9y	OW/OB 9y
Maternal	**1.20 (1.02, 1.47)***	1.01 (0.91, 1.12)	1.15 (0.94, 1.40)	1.14 (0.92, 1.41)	0.96 (0.85, 1.09)	0.87 (0.71, 1.06)	0.94 (0.82, 1.08)	1.21 (0.97, 1.51)	0.93 (0.75, 1.16)	1.07 (0.90, 1.27)
Paternal	1.34 (0.71, 2.53)	0.89 (0.71, 1.11)	0.87 (0.56, 1.37)	0.85 (0.63, 1.15)	1.05 (0.86, 1.27)	0.76 (0.54, 1.06)	**1.03 (1.01, 1.19)***	1.20 (0.83, 1.73)	0.62 (0.41, 1.93)	0.87 (0.83, 1.92)
MGM	0.89 (0.56, 1.43)	**1.35 (1.02, 1.79)***	0.99 (0.63, 1.56)	1.05 (0.69, 1.59)	1.04 (0.85, 1.29)	1.11 (0.84, 1.49)	1.18 (0.84, 1.67)	1.72 (0.81, 2.93)	0.73 (0.41, 1.28)	1.16 (0.80, 1.70)
MGF	0.55 (0.28, 1.08)	0.84 (0.64, 1.11)	0.54 (0.24, 1.19)	0.63 (0.30, 1.29)	0.93 (0.70, 1.23)	1.02 (0.76, 1.36)	1.00 (0.99, 1.02)	1.03 (0.99, 1.07)	0.97 (0.93, 1.01)	0.99 (0.96, 1.03)
PGM	0.81 (0.33, 1.99)	0.93 (0.68, 1.26)	0.82 (0.24, 1.87)	1.31 (0.69, 2.49)	0.92 (0.75, 1.13)	1.03 (0.95, 1.54)	**1.07 (1.05, 1.09)***	0.97 (0.94, 1.01)	0.98 (0.95, 1.02)	**1.13 (1.01, 1.90)***
PGF	1.36 (0.49, 3.79)	1.74 (0.84, 3.61)	2.00 (0.49, 8.20)	0.71 (0.34, 1.49)	1.07 (0.75, 1.52)	0.84 (0.63, 1.12)	1.11 (0.77, 1.61)	0.93 (0.60, 1.43)	0.99 (0.59, 1.66)	0.94 (0.63, 1.39)

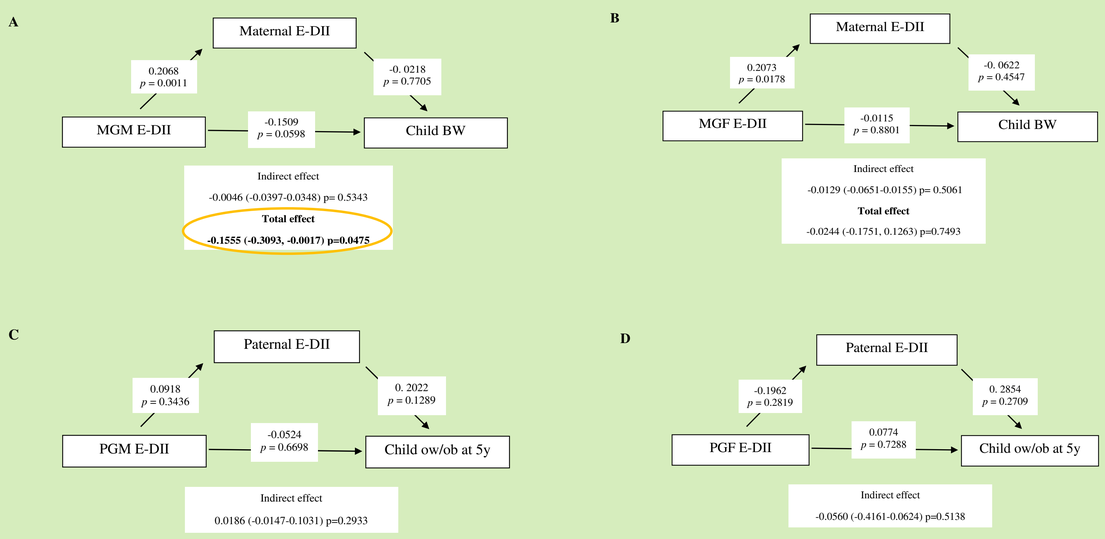
[1]Values are OR (95% CI) expressed for 10-point increment of E-DII scores for continuous analysis. *p<0.05

4.3. Mediation analysis

Mediation analysis was conducted to assess the degree to which the reported relationships between grandparental E-DII scores and grandchild's birth and childhood outcomes were mediated via the parental E-DII scores (**Figure 1**):

- Examination of the association between MGM E-DII scores and grandchild's birthweight (**Fig. 1A**) revealed a significant total effect (β: -0.1555 (-0.3093, -0.0017) *p*=0.048).
- **Fig. 1B** shows the possible effects of MGF E-DII scores on grandchild's birthweight, but these are not significant.
- Direct effects were observed between MGM and MGF E-DII scores on maternal E-DII scores (β: 0.2068, *p*=0.0011 and β: 0.2073, *p*=0.02, respectively) (**Fig. 1A, 1B**).
- In the paternal line (**Fig. 1C, 1D**), no significant associations were observed for paternal GP E-DII scores on grandchild's overweight and obesity status at 5 years with paternal E-DII scores as mediator.

Figure 1. Mediation analysis of grandparental E-DII scores on grandchild outcome through parental E-DII scores



5. CONCLUSIONS

Our study makes a significant and novel contribution to the scarce literature and demonstrates that parental dietary inflammation is associated with adverse offspring birth outcomes and childhood adiposity. The findings, which suggest **a specific *in utero* influence of antenatal maternal dietary inflammation and a specific post-natal influence of paternal line dietary inflammation on childhood adiposity**, merit further investigation.

References

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