PLACENTAL FATTY ACID PROFILE, DNA METHYLATION AND ADVERSE METABOLIC OUTCOMES IN THE OFFSPRING AT SCHOOL AGE

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BACKGROUND

The placenta plays a key role in regulating fatty acid (FA) transport from maternal to fetal circulation. An unfavourable FA profile in the placenta, reflecting an inadequate nutritional status during pregnancy, may cause changes in placental DNA methylation and negatively affect fetal growth and metabolic health of the offspring.

AIMS

To study the association of an unfavourable placental FA profile with:
1) placental DNA methylation of specific genes related to pre and postnatal growth.
2) anthropometric and metabolic parameters of the offspring at school age.

METHODS

In a prenatal cohort of 81 pregnant women-newborns pairs, placental FA profile was determined by gas liquid chromatography and DNA methylation of the regulatory region of *C19MC, ZNF331* and *IGF2/H19* placental imprinted domains (imprinting control region; ICR) was determined by pyrosequencing. Newborns were followed up until school age (6 years, n=37) when anthropometric (weight, BMI, body composition metabolic) and metabolic (serum lipids, glucose, HbA1C, HOMA-IR) parameters were assessed.

RESULTS

An unfavourable FA profile [increased levels of saturated FA and omega-6 and decreased levels of omega-3] was associated with hypomethylation of *C19MC* and hypermethylation of *ZNF331* and *IGF2/H19* genes (all p<0.05; Figure 1). Such unfavourable FA profile was also associated with increased visceral fat, total fat mass, glucose and HbA1C in the offspring at age 6 years (all p<0.05; Table 1) and was a risk factor for increased visceral fat (odds ratio: 2.5; 95% CI: 1.2-5.9) (Table 2).

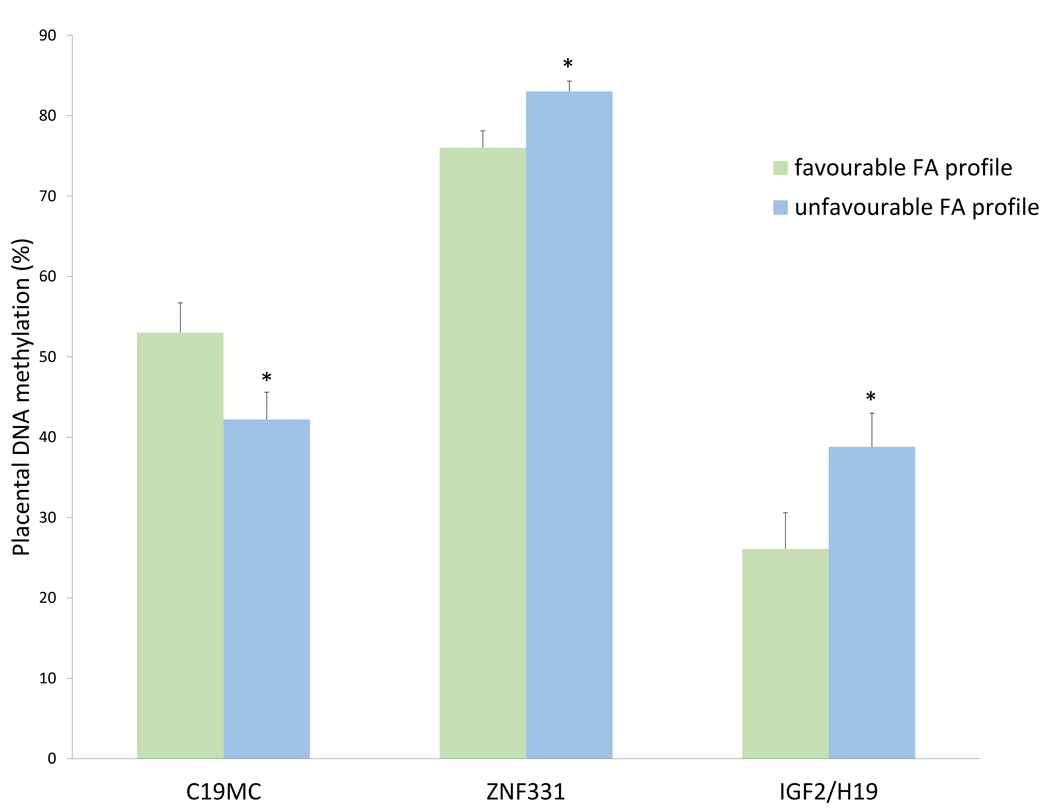

Figure 1: Placental DNA methylation of *C19MC, ZNF331* and *IGF2/H19* genes.

Table 1: Clinical characteristics of the children.

	Favourable FA profile	Unfavourable FA profile	p-value
Newborn parameters	**n=38**	**n=43**	
Sex (% girls)	44	40	Ns
Gestational age (weeks)	40 ± 0.1	40 ± 0.2	Ns
Birth weight SDS	1.0 ± 0.1	1.0 ± 0.1	Ns
Birth height SDS	-0.3 ± 0.1	-0.0 ± 0.1	Ns
Placental weight (g)	636.7 ± 26.7	611.7 ± 16.4	Ns
Follow-up parameters	**n=18**	**n=19**	
Age (years)	5.9 ± 0.2	6.3 ± 0.1	Ns
Weight SDS	0.1 ± 0.1	0.4 ± 0.3	Ns
Height SDS	0.1 ± 0.2	-1.0 ± 1.4	Ns
BMI SDS	0.1 ± 0.2	0.2 ± 0.2	Ns
Visceral fat (cm)	5.0 ± 0.2	5.9 ± 0.2	0.02
Fat mass (%)	22.0 ± 1.9	25.9 ± 2.0	0.05
Glucose (mg/dL)	84.0 ± 2.0	85.8 ± 1.4	0.02
HbA1C (%)	5.0 ± 0.05	5.2 ± 0.07	0.04
Insulin (mIU/L)	5.2 ± 0.6	6.3 ± 0.7	Ns
HOMA-IR	1.0 ± 0.1	1.3 ± 0.2	Ns
TG (mg/dL)	54.3 ± 4.1	44.9 ± 2.1	Ns
HDL-c (mg/dL)	55.6 ± 2.5	56.1 ± 3.0	Ns

Table 2: Odds Ratio for visceral fat (>50th centile) in the offspring.

Visceral fat > 50th centile	p-value	95% CI	
		Lower	Upper
Favourable FA profile	0.412	0.184	0.923
Unfavourable FA profile	2.471	1.201	5.976

CONCLUSION

The placental FA profile associated with DNA methylation levels of specific genes related to pre and postnatal growth and metabolic parameters of the offspring at school age. Such FA profile may be used to identify those newborns at higher-risk to develop metabolic diseases later in life.