

Ghrelin and GHSR1 receptor in placenta of SGA, LGA and AGA newborns

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INTRODUCTION

Intrauterine growth is a biological process regulated by maternal, placental and fetal endocrine signals. Birth weight is an indicator of the health of the newborn. Alterations in fetal growth lead to perinatal health risks and favor metabolic diseases during adult life. Therefore the study of endocrine factors determining birth weight, such as ghrelin is an important issue. Ghrelin may exist as two molecular forms, desacyl ghrelin (DAG), and acyl ghrelin (AG). Current evidence showed to DAG as an active hormone with effects on different tissues in diverse physiological and pathophysiological states. Although cord blood (CB) ghrelin levels have been correlated to birth weight, it is unknown which ghrelin's molecular variants are involved and if expression and methylation of ghrelin receptor (GHSR1) has a key role in fetal development.



OBJETIVE

To analyze total ghrelin, acyl ghrelin (AG), and desacyl ghrelin (DAG) in CB of newborns small (SGA), appropriate (AGA) and large (LGA) for gestational age, and to evaluate expression and methylation of placental GHS-R1.

RESULTS

Table 1. Characteristics of mothers and newborns with small (SGA), adequate (AGA) and with large weight for gestational age (LGA).

	SGA (n = 20)	AGA (n = 20)	LGA (n = 20)	ANOVA (F)/ Chi ² (H)*	p
Newborns					
Gestational age (weeks)	38.2 ± 1.1	38.7 ± 1.1	39 ± 0.9	6.1	0.0040
Birth weight (g)	2297 (2089- 2403)	3273 (2915-3358)	3915 (3815-4168)	52.5*	<0.0001
Birth length (cm)	45.7 ± 2.5	50.9 ± 2.0	52.7 ± 2.1	53.6	<0.0001
Cephalic perimeter (cm)	32.2 ± 1.6	34.7 ± 1.6	36.5 ± 1.3	39.6	<0.0001
Thoracic perimeter (cm)	30 (28-31)	34 (32-34)	35 (35-37)	45.4*	<0.0001
Abdominal perimeter (cm)	27.3 ± 2.0	30.8 ± 1.6	34.1 ± 2.2	60.2	<0.0001
Glucose (mg/dl)	64.0 ± 20.7	74.7 ± 14.4	65.1 ± 10.9	2.8	0.0716
Triglycerides (mg/dl)	52 (37-68)	58 (51-63)	48 (44-56)	6.2*	0.0444
Cholesterol (mg/dl)	74.8 ± 15.9	84.4 ± 15.5	74.9 ± 14.2	2.6	0.0823
Pregestational weight (Kg)	54.9 ± 10.6 □	57.1 ± 9.3 ¥	75.9 ± 20.8	11.7	<0.0001
Pregestational BMI (Kg/m ²)	22.5 (20.3-27.5) □	24.2 (20.6-26.1)	28.8 (25.1 - 31.1) □	8.9*	0.0115
Weight gain at pregnancy (kg)	12.0 (10 - 13)	12.2 (10 - 17.6)	12.0 (10 - 15)	2.1*	0.3495
Placental weight (g)	400 ± 64 □	610 ± 24	751 ± 119	60.6	<0.0001
Glucose (mg/dl)	76.2 ± 14.4	80.8 ± 12.7	77.4 ± 14.3	0.6	0.5461
Hemoglobin A1c %	5.2 ± 0.7	5.4 ± 0.7	5.5 ± 0.8	0.8	0.4194
Triglycerides (mg/dl)	199.5 ± 61.8	236.4 ± 57.8	232.2 ± 73.2	1.9	0.1519
Cholesterol (mg/dl)	199.8 ± 41.5	208.4 ± 29.1	204.1 ± 43.9	0.2	0.7837
Mothers					

SUBJECTS AND METHODS

Interview with Mother (18-35a).
Letters:
❖ Information.
❖ Informed consent.

Data Collection

Newborns SGA, AGA y LGA

Sample Collection

Venous blood of Mothers

Blood of umbilical cord (UC)

Placenta (5x5 cm)

Glucose
Hemoglobin A1c
Triglycerides
Cholesterol

Glucose
Triglycerides
Cholesterol
ELISA:
Total ghrelin
AG
DAG

Expression of GHSR1
Immunodetection

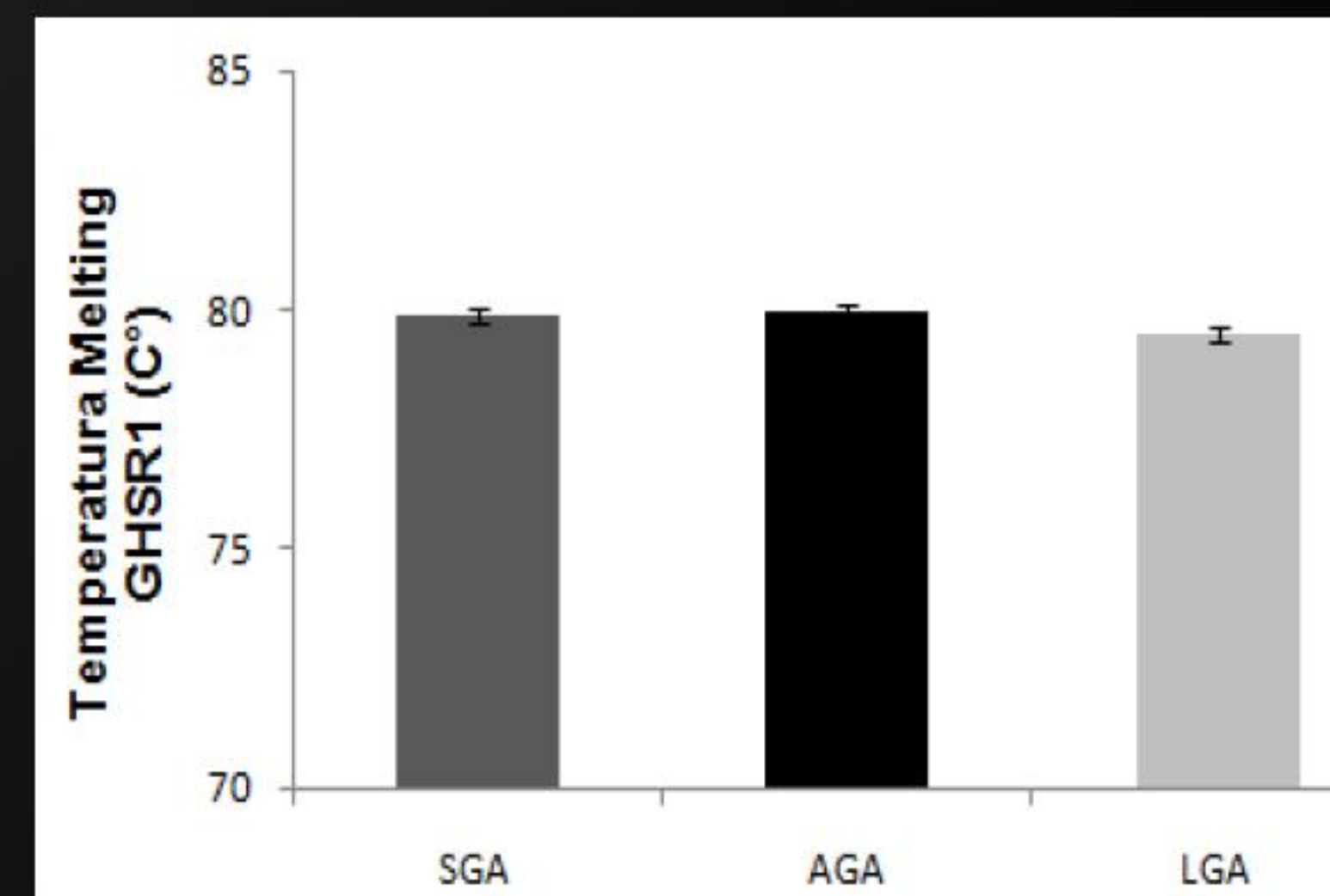


Figure 1. Melting temperature of the amplification products for the GHSR1 gene of the SGA group (79.9 ± 0.16 °C), AGA (80.0 ± 0.15 °C) and LGA (79.5 ± 0.19 °C). NS difference.

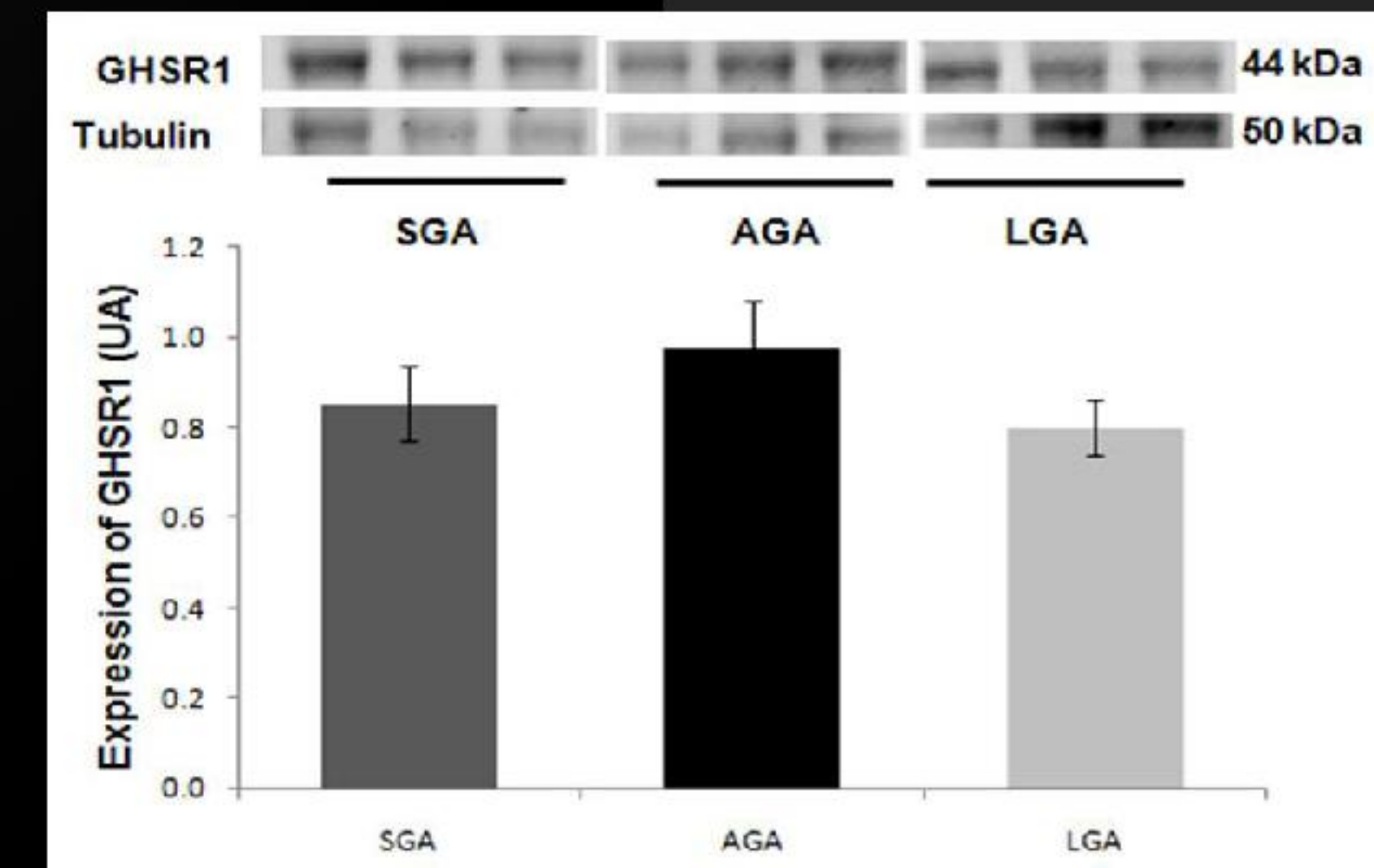


Figure 2. Expression of GHSR1. Immunoblotting of receptor GHSR1 and immunoblotting of tubulin on nitrocellulose membrane. Expression of the ghrelin receptor in the groups SGA (0.85 ± 0.08 UA), AGA (0.97 ± 0.1 UA) and LGA (0.8 ± 0.06 UA), NS difference.

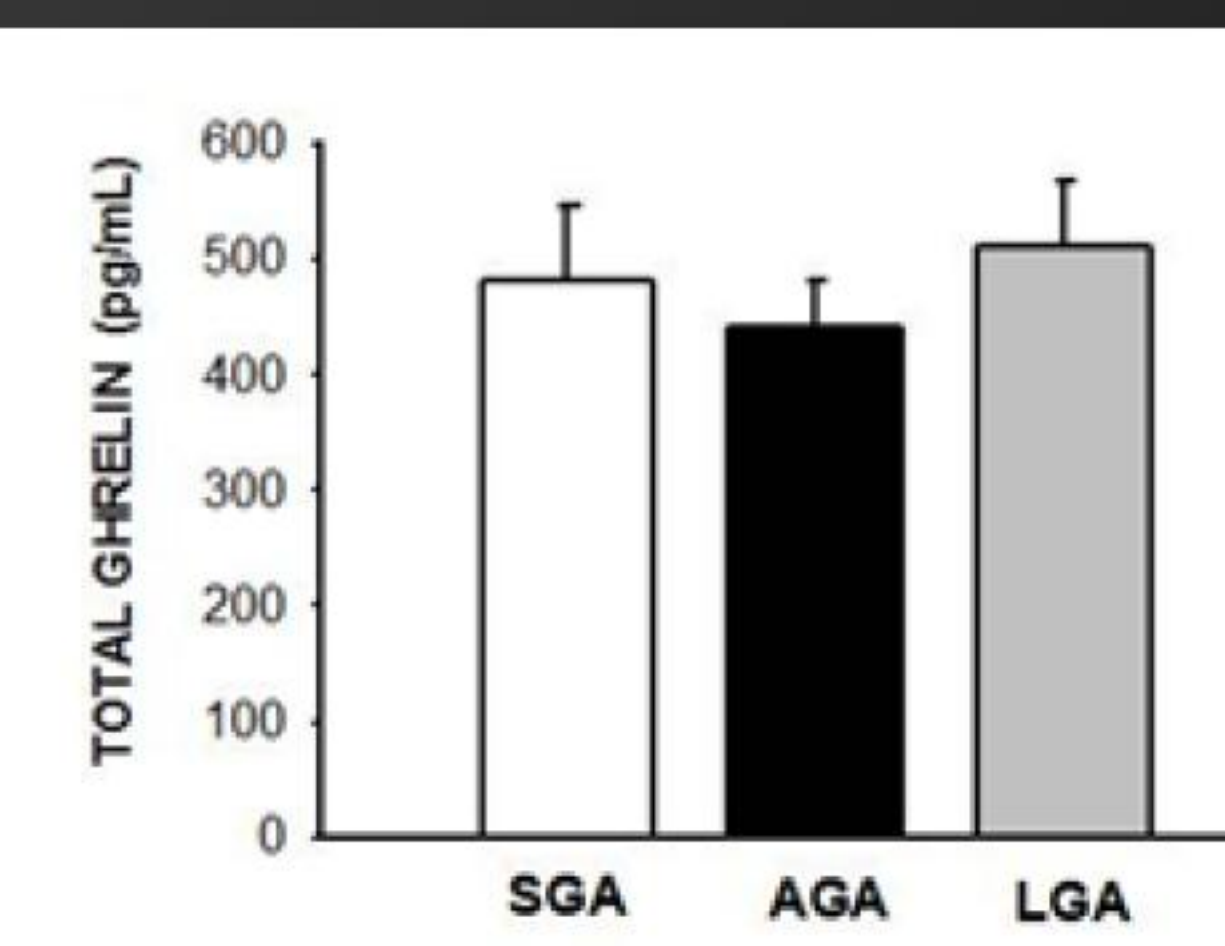


Figure 4. Total ghrelin levels in umbilical cord in the SGA 495.1 ± 58.7 pg/mL, AGA (428.7 ± 37.7 pg/mL) y LGA (445.0 ± 42.2 pg/mL). NS difference.

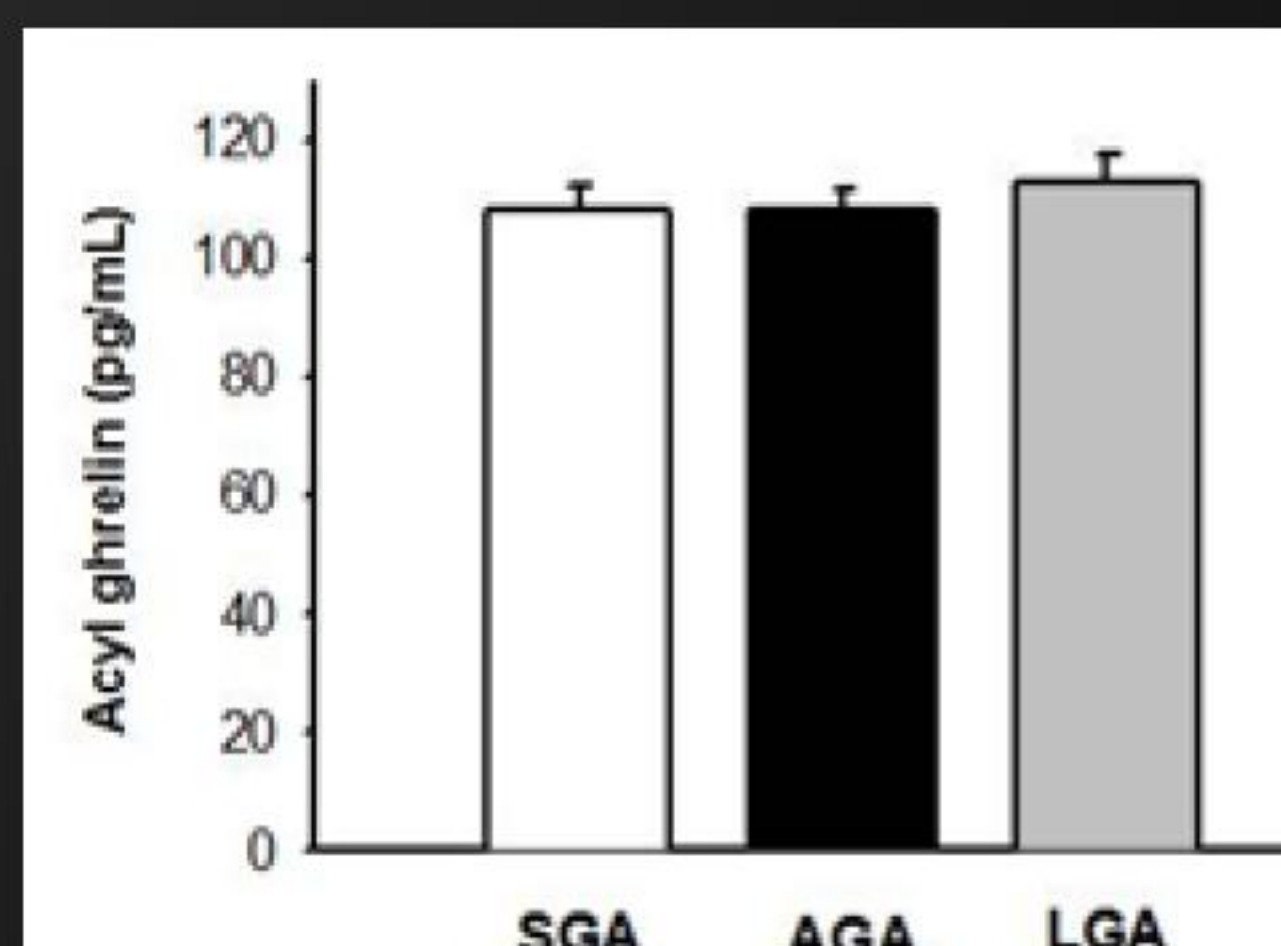


Figure 4. AC levels in umbilical cord in the SGA 108.2 ± 19.3 pg/mL, AGA (108.0 ± 16.6 pg/mL) y LGA (112.9 ± 20.0 pg/mL). NS difference.

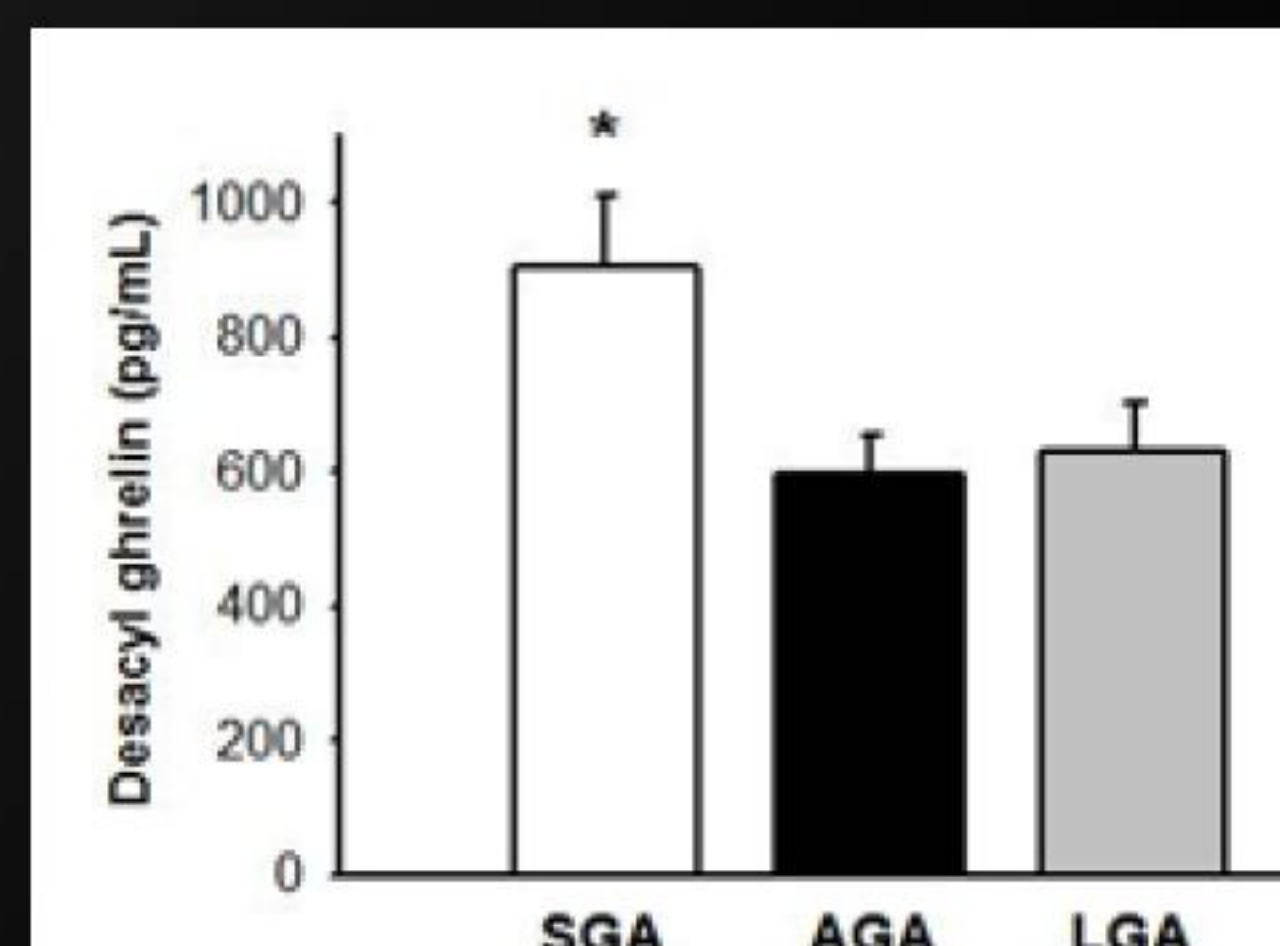


Figure 4. DAG levels in umbilical cord in the SGA 902.1 ± 109.1 pg/mL, AGA (597.4 ± 58.2 pg/mL) y LGA (627.2 ± 76.4 pg/mL). p=0.03

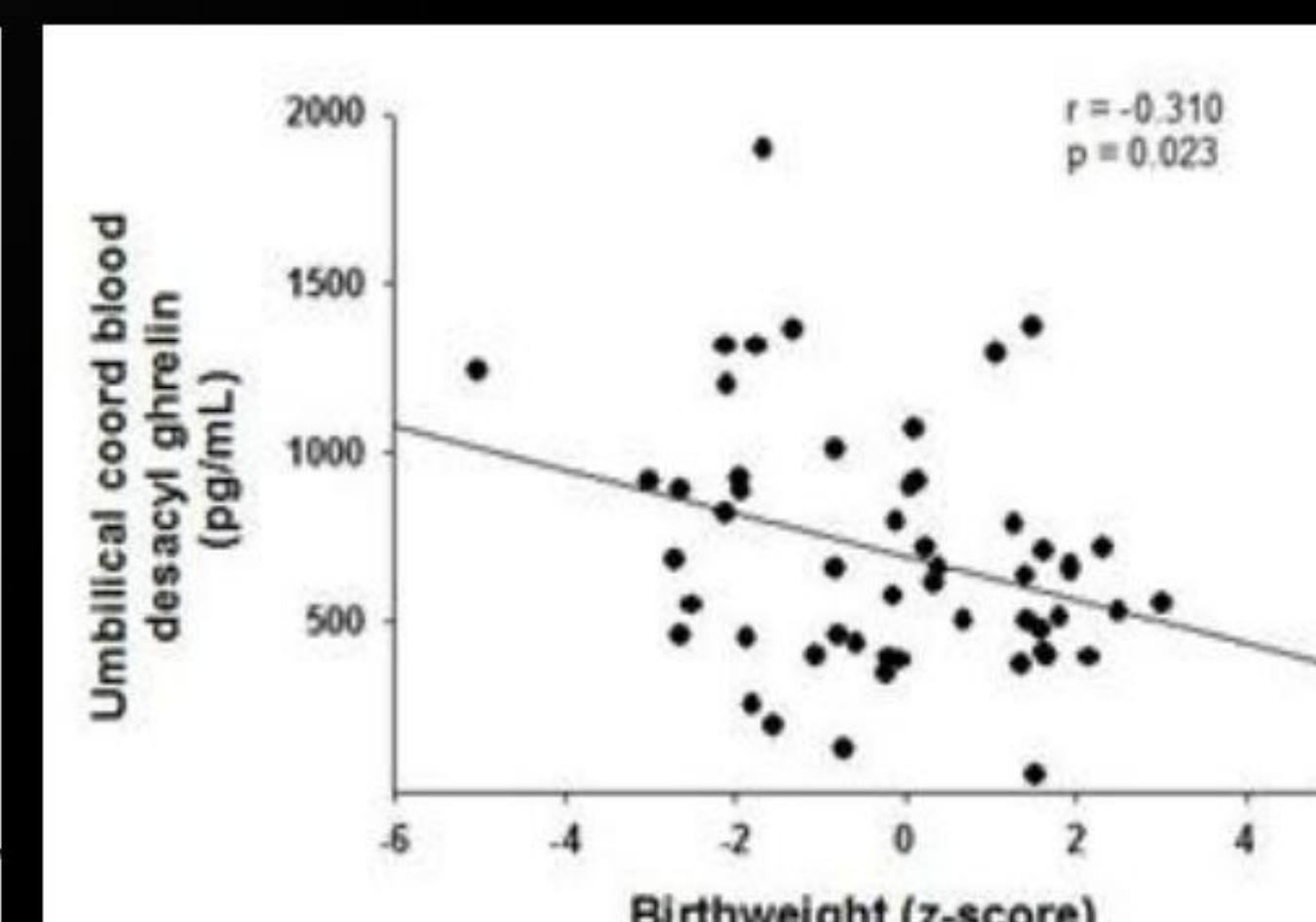


Figure 6. Correlation between birth weight and DAG levels. P-Value 0.023.

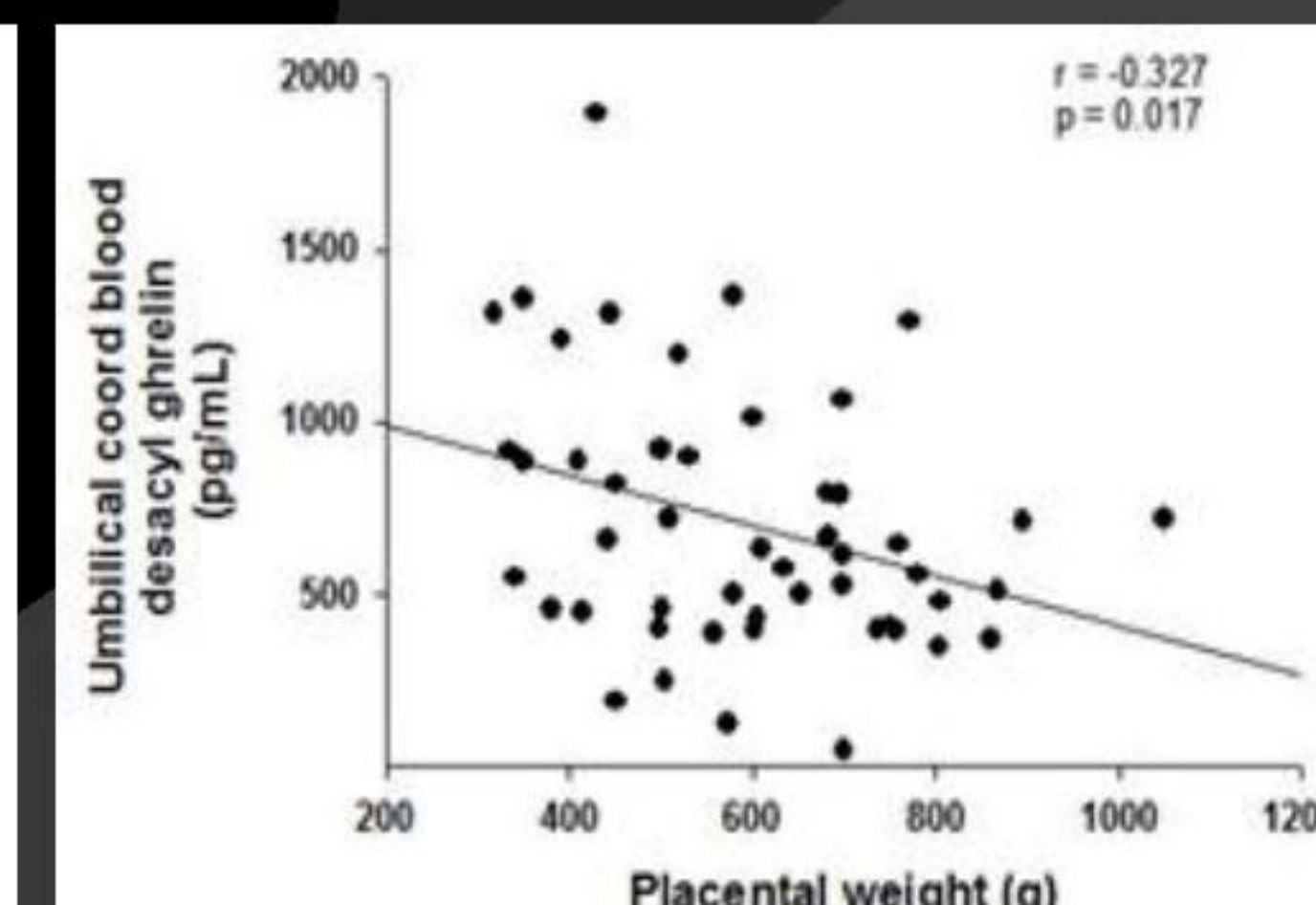


Figure . Correlation between placental weight and DAG levels. P-Value 0.017

CONCLUSIONS

Our results showed that expression and methylation of ghrelin receptor (GHSR1) has unrelated with birth weight. Suggesting that additional factors, such as DAG, are involved in the mechanism that determines birth weight.

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