

Placental Glucose Transporter Expression in Pregnancies with Early and Late-Onset Fetal Growth Restriction

Muhammad Pradhiki Mahindra^{1,2}, Sara Hillman^{1,2}, Dimitrios Siassakos^{1,2}, Kasia Maksym^{1,2}, Anna David^{1,2}, Owen Vaughan¹

1 Maternal Fetal Medicine Department, Elizabeth Garrett Anderson Institute for Women’s Health, University College London

2 Elizabeth Garrett Anderson Wing, University College London Hospitals NHS Foundation Trust



Introduction:

Maternal to fetal nutrient transfer is dependent on maternal glucose levels, glucose concentration gradient, placental glucose utilization, and placental glucose transporter (GLUT) activity. The correlation between GLUT expression and fetal growth restriction (FGR) remains poorly understood.

Study Objective: To evaluate the expression of *GLUT 1*, *3*, *4*, *8*, *9*, and *12* in the placentas born to pregnancies with early and late-onset FGR compared to appropriate growth (AGA) fetus.

Methods:

Participant recruitment at University College London Hospitals (UCLH) with informed consent and ethical approval:

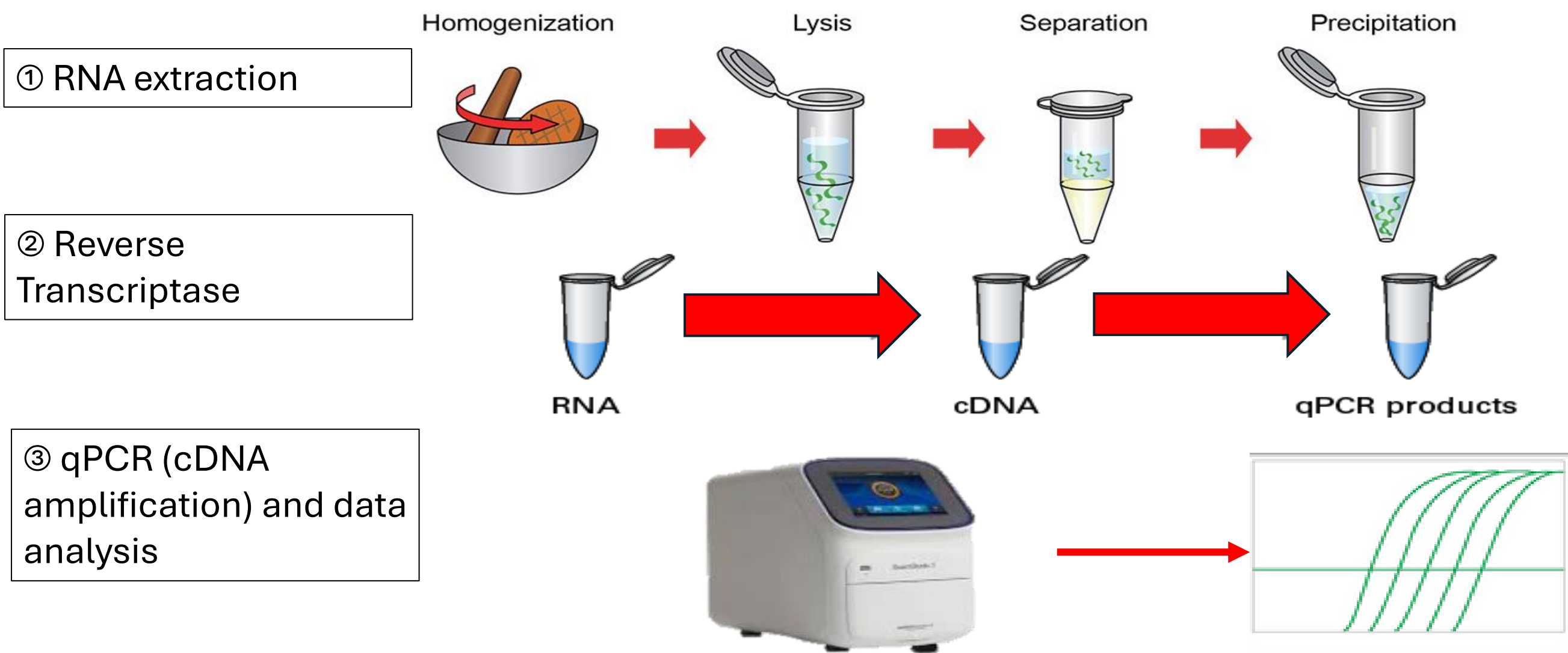
- Early FGR : Estimated fetal weight (EFW) < 600 grams and < 3rd centile, between 20 and 30 + 6 weeks of gestation.
- Late FGR : EFW < 10th centile after 32 weeks of gestation with a history of the normal-sized fetus at the mid-gestation scan.
- Control : Women with normal glucose tolerance and appropriate growth fetus.

Placentas were collected from 9 controls , 14 early FGR women, and 5 late FGR women

1 x 1 cm cubes of villous tissue were snap-frozen using liquid nitrogen and stored at -80°C.

RT-qPCR was performed to determine *GLUT* gene expression relative to endogenous controls:

Statistical analysis was performed using a one-way ANOVA test (numerical data) and Chi-square (categorical data) between study groups (early FGR, late FGR) and control group.

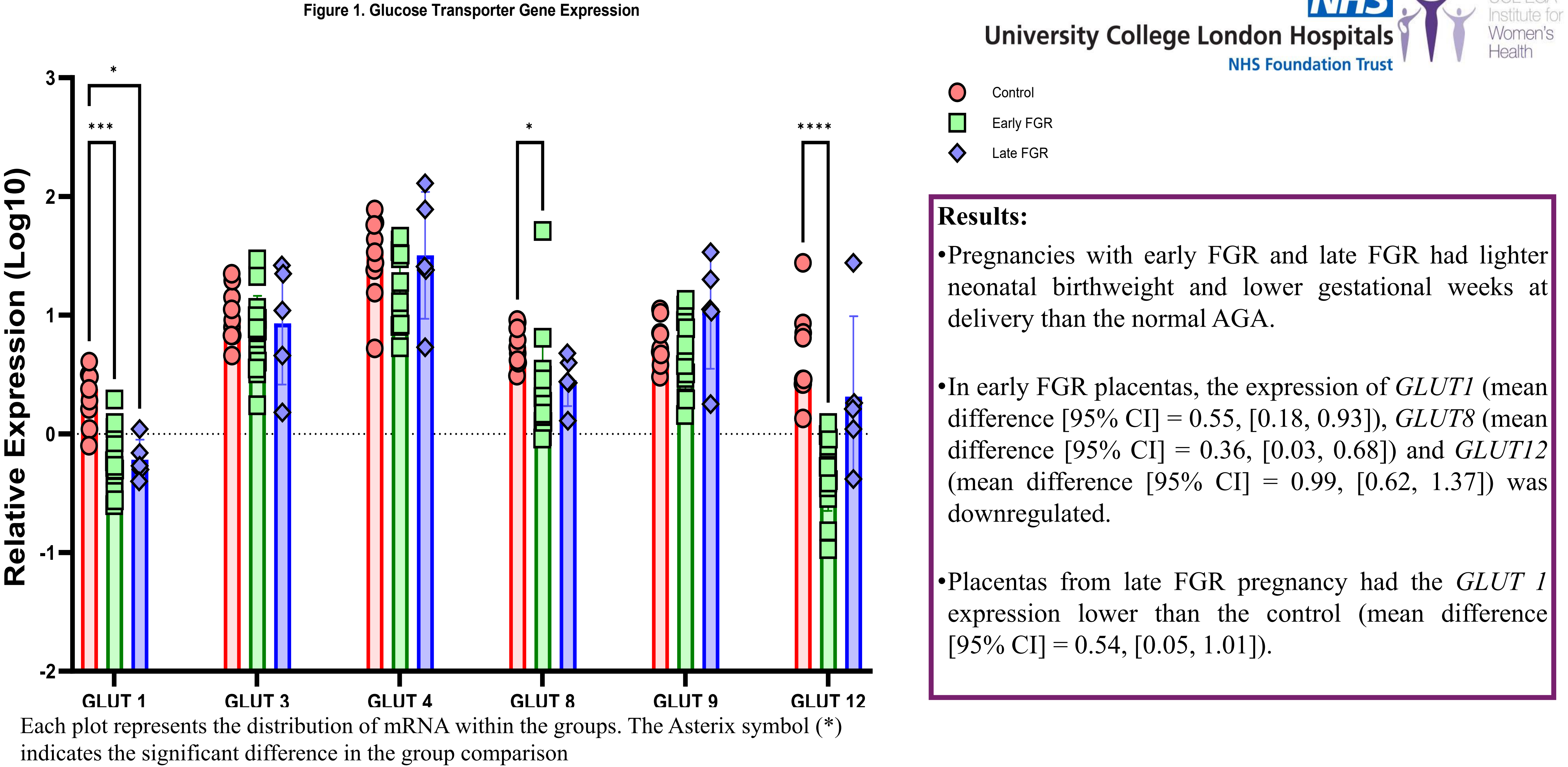


	Control (n = 9)	Early FGR (n = 14)	Late FGR (n = 5)
Maternal Characteristics			
Age (Years)	35.44 ± 4.87	35.79 ± 5.5	30 ± 7.2
Maternal BMI	26.33 ± 5.0	26.64 ± 4.60	27.20 ± 8.15
Gestational weeks at delivery	39.12 ± 0.78	29.57 ± 3.91**	36.60 ± 2.30*
Cesarean section/ vaginal delivery	8/1	13/1	3/2
Pregnancy Complications			
Preeclampsia	0 (0)	5 (35.7)	1 (20)
Premature Birth	0 (0)	14 (100)**	1 (20)
Fetal-Neonatal Outcomes			
Male/ female	7/2	5/9	2/3
Neonatal Birthweight (grams)	3459 ± 372.56	961 ± 588.83**	2169 ± 435.55**

Table 1. Maternal and Neonatal Characteristics of Study Participants

Data are presented as mean ± SD, or proportion (%).
* = p-value < 0.01, ** = p-value < 0.01.

FGR = fetal growth restriction ;
GA = gestational age;



Results:

- Pregnancies with early FGR and late FGR had lighter neonatal birthweight and lower gestational weeks at delivery than the normal AGA.
- In early FGR placentas, the expression of *GLUT1* (mean difference [95% CI] = 0.55, [0.18, 0.93]), *GLUT8* (mean difference [95% CI] = 0.36, [0.03, 0.68]) and *GLUT12* (mean difference [95% CI] = 0.99, [0.62, 1.37]) was downregulated.
- Placentas from late FGR pregnancy had the *GLUT 1* expression lower than the control (mean difference [95% CI] = 0.54, [0.05, 1.01]).

Discussion:

- Pregnancy with FGR mainly lowered the expression of the *GLUT 1* gene. In early FGR, *GLUT8* and *GLUT 12* genes were also affected.
- This study did not measure the abundance of placental glucose transporter proteins.
- The findings may help us understand how pregnancy conditions affect the placental glucose transport function to underlie abnormal fetal growth and neonatal birthweight.

Conclusion:

- GLUT 1 is an important determinant for fetal growth in pregnancy affected by FGR. In early FGR, GLUT 8 and 12 expression was downregulated compared to control.
- Placental GLUTs may be potential diagnostic and therapeutic biomarkers for pregnancies affected by FGR.

References:

- Owen R. Vaughan, Anna David et al; Placenta-specific *Slc38a2*/SNAT2 knockdown causes fetal growth restriction in mice. *Clin Sci (Lond)* 17 September 2021; 135 (17): 2049–2066.
- EVERREST Consortium. EVERREST prospective study: a 6-year prospective study to define the clinical and biological characteristics of pregnancies affected by severe early onset fetal growth restriction. *BMC Pregnancy Childbirth*. 2017 Jan 23;17(1):43.
- Stanirowski PJ et al. Impact of pre-gestational and gestational diabetes mellitus on the expression of glucose transporters GLUT-1, GLUT-4 and GLUT-9. *Endocrine*. 2017;55:799–808.