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Carbohydrate Overnutrition Harmful to both Obese Pregnant Mice and Fetuses

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ABSTRACT

***Background**: Obesity in pregnancy due to carbohydrate overnutrition is still rarely reported, and the incidence of obesity in pregnancy in developing countries has begun to increase. This study aims to observe the detrimental effect of obesity in mothers and developing fetuses of mice fed a high carbohydrate diet. **Methods**: The obese group was fed a high carbohydrate (HC) diet, and the control group had a standard diet for 12 weeks. All mice were mated until they were pregnant and terminated for blood collection every trimester. Seven mice from the obese group and 7 mice from the control group were followed until 3rd trimester and then terminated for blood collection. Blood lipid profile and glucose were examined by photometrics, while anthropometric variables were measured by weight scale and meter scale. **Results**: Maternal obesity was associated with significantly elevated blood triglyceride levels in the first and second trimesters. At the same time, no significant differences were observed in blood glucose, total cholesterol, HDL, and LDL levels between the obesity and normal weight groups in the third trimester. Furthermore, fetuses of obese mothers exhibited significantly increased birth weight, length, head circumference, and waist circumference compared to those of normal-weight mothers. **Conclusion**: Obesity in pregnancy due to carbohydrate overnutrition could have detrimental effects on both the mother and developing fetuses.*

1. INTRODUCTION

Obesity has become a significant problem worldwide, including obesity in pregnancy.[1,2] Obesity in pregnancy has many detrimental effects on both the mother and developing fetuses in the uterus, as the risk for future childhood. Hypertension in pregnancy, cesarean section delivery, macrosomia, and obesity in childhood are among the effects of obesity in pregnancy that have always been reported.[3,4,5]

In developed countries, obesity is commonly due to high-fat consumption and leads to metabolic diseases in both mothers and fetuses.[6,7] Inversely, in developing countries, high carbohydrate consumption may cause obesity in pregnancy [8,9] and has a negative impact on both mother and fetus and maybe by different mechanisms. Excessive carbohydrates because of high glycemic index could interfere with the metabolic status of pregnant mothers.[10,11]

It is believed that high levels of glucose and profile lipid alteration are the underlying mechanisms that lead to negative influence for both mothers and fetuses in high-fat diet.[12,13,15] There are limited studies focused on carbohydrate nutrition on obesity in pregnancy and their impact on mothers and fetuses, and we hypothesized that obesity in pregnancy due to carbohydrate overnutrition alone could have a detrimental effect on both mothers and fetuses, as shown in high-fat diet as well.

The objective of this study is to observe the detrimental effect of obesity in both mother and developing fetuses of mice fed a high carbohydrate diet.

2. METHODS

Animal

Mus musculus females were maintained in the Animal Laboratory of the Medical Faculty of Hasanuddin University. All mice were maintained at 28-30^{o}C temperature on a 12 h light and 12 dark cycles. Female mice, 8 weeks of age with a weight of 15-16 grams, were divided into two groups. Group 1 was fed a high carbohydrate (HC) diet, and Group 2 was the standard diet for 12 weeks. All mice in group 1 with a weight > 36 grams (obesity group) and in group 2 with a body weight < 25 grams (normal weight group) were recruited in this study. All groups mated until they were pregnant and terminated for collecting blood with cardiac puncture every trimester for examining blood glucose and triglyceride. Furthermore, 7 mice from the obese group and 7 mice from the control group were followed until 3rd trimester and then terminated to collect the blood lipid profile and examine the fetuses' anthropometry. In this study, the duration from the animal to be pregnant (fertilization) until delivery is about 21-23 days, and every trimester consists of 7 days. All protocols for this study were accepted by Hasanuddin University's Medical Faculty Ethical Board, with the registered number UH14070398.

Diet

The mice were fed by HC for the obese group and standard diet for the control group. The HC diet consists of carbohydrate 75%, fat 5%, protein 17%, and vitamin 1%, while the standard diet consists of carbohydrates 5%, fat 4%, protein 19%, calcium 0,5-1,1%, and phosphor 0,5-0,7 1%. The HC diet was produced by the Nutrition Department,

Animal Husbandry Faculty of Hasanuddin University, and the standard diet was bought from the animal diet market.

Laboratory assays

Lipid profiles such as triglycerides, LDL, and HDL were measured with enzymatic photometric technique (ABX Pentra 400) in Makassar District Health Laboratory. The colorimetric indicator is quinoneimine which is generated from 4-aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of peroxidase (Trinder's reaction). Blood glucose is examined by a glucometer kit (Accu-check) with an enzyme on the Accu-check strip that converts the glucose in the blood sample to gluconolactone. Anthropometry status was determined by using a digital weight scale (Furi FEC 150) and a tailor-meter scale.

Statistical analysis

All data were normally distributed and were shown as mean ± standard deviation of the mean. An independent sample t-test was used to compare body weight, blood glucose, and TG level every trimester, lipid profile, and anthropometric measurement in 3rd trimester between group 1 and group 2. Paired t-test was also used to compare the change of blood glucose and triglyceride every trimester in group 1 and group 2 mice.

3. RESULTS

Table 1. The animal's body weight in each trimester before terminated

	Obese group (gr)	Control group (gr)	p
	Mean ± SD	Mean ± SD	
Trimester 1	41.5 ± 2.11	27.9 ± 0.98	< 0.001
Trimester 2	51.4 ± 0.97	37.3 ± 3.27	< 0.001
Trimester 3	59.0 ± .10	42.0 ± 1.37	< 0.001

p : Independent sample t-test

The data showed (Table 1) that the body weight before termination increased significantly (p<0,05) in the obese group compared to the control group as well. The HC diet was successful in increasing the weight body of the experimental animal as expected.

Table 2. Blood glucose and triglyceride levels in the obese group and the control group during pregnancy

Variables	Obese group (n = 16)	Control group (n = 18)	**p**
Glucose (GDS) mg/dl	Mean ± SD	Mean ± SD	
Trimester 1	181.0 ± 48.51[a]	184.7 ± 29.24[c]	0.880
Trimester 2	172.2 ± 40.18[a]	217.3 ± 98.06[c]	0.321

Trimester 3	188.8 ± 61.42[a]	203.8 ± 56.63[c]	0.683
Triglyceride (TG) mg/dl			
Trimester 1	118.2 ± 22.03[b]	78.0 ± 17.47[d]	0.008*
Trimester 2	117.5 ± 32.92[b]	66.8 ± 18.90[d]	0.008*
Trimester 3	178.0 ± 79.67[b]	114.3 ± 62.12[d]	0.154

* *Independent sample t-test p<0.05* , n = number of mice
a,b,c,d superscript for Paired t-test, p > 0.05 for same superscript

Table 2 showed an alteration of glucose and triglyceride serum levels every trimester in both groups. Triglyceride serum, particularly in 1st trimester and 2nd trimester, increased significantly (Independent sample t-test, p = 0,008) in the obesity group, but blood glucose levels did not change significantly in both groups. No significant difference (Paired t-test) for blood glucose and triglyceride changed every trimester.

Table 3. Third trimester of pregnancy of lipid profiles and fetuses anthropometric in the obese group and the control group

Variables	Obese group (n=7)	Control group (n=7)	p
Lipid Profile	Mean ± SD	Mean ± SD	
Cholesterol (mg/dl)	68.0 ± 21.49	84.4 ± 33.90	0.300
HDL (mg/dl)	36.9 ± 12.03	40.4 ± 16.23	0.648
LDL (mg/dl)	6.6 ± 1.13	11.7 ± 8.08	0.121
TG (mg/dl)	191.4 ± 89.3	164.4 ± 102.89	0.609
Fetuses anthropometric			
BW (gr)	1.4 ± 0.18	0.6 ± 0.08	< 0.001*
BL (mm)	2.4 ± 0.11	1.9 ± 0.15	< 0.001*
HC (mm)	3.0 ± 0.22	2.4 ± 0.11	< 0.001*
WC (mm)	2.8 ± 0.19	2.2 ± 0.07	< 0.001*
AC (mm)	0.9 ± 0.07	0.9 ± 0.05	0.109

** Independent sample t test*

BW : bodyweight, BL : Bodylenghts; HC : Head circumference; WC : Waist circumference; AC : Arm circumference

Lipid profile in 3rd trimester did not differ significantly. Still, anthropometric variables were substantially higher (Independent sample t-test, p< 0,05), except arm circumferences, in fetuses from the obesity group, as shown in Table 3.

4. DISCUSSIONS

Our data showed that carbohydrate overnutrition leads to obesity in mice, increases triglyceride (TG) serum, especially in the first and second trimesters, and increases the anthropometric size of fetuses. These data are in line with many studies

reported before, although obesity in those studies due to high-fat nutrition or high-fat and high-carbohydrate nutrition. [15,16,17,18]

Blood glucose did not differ between the obese and the control groups in every trimester, although we found a raised anthropometric size in the obese group. In diabetic pregnancy, blood glucose was believed to have a strong role in increasing the fetus size, [19,20] but in obese persons, the data was still scarce. This study revealed that blood glucose was not associated with macrosomia in the fetuses. This data is in line with mice fed high fructose, whose blood glucose was the same as those fed a standard diet. [21] However, in another study, [22] by using a fructose diet for mice, the blood glucose and body weight were increased compared to control mice.

In this study, we used a diet with carbohydrates (not fructose) and a lack of data about diets high in carbohydrates alone for mice, especially for pregnancy outcomes. To our knowledge, this is one of the very limited studies obtained to examine the detrimental effect of high carbohydrate nutrition alone on both mother and fetus size. The data showed that the detrimental effect also persisted in fetuses, as did the effect of a high-fat diet.

Blood lipid profiles such as cholesterol, HDL, LDL, and TG did not differ in 3rd trimester in the obese group compared to the control group (table 3), but TG tended to increase every trimester and was significantly higher in 1st trimester and 2nd trimester in the obesity group (table 2). The ascending of TG leads to an increase in the anthropometric size of fetuses in obese mice. TG also reported induced macrosomia (large of gestational age) and produced hypertension in gestational females.[23,24] Furthermore, a higher level of TG in early gestational age was associated with gestational diabetes mellitus (GDM), which produced macrosomia and is also related to cardiovascular risk for mothers. [25,26]

The increased level of TG, without being followed by blood glucose in our data, may be a special alteration in terms of a carbohydrate-over-nutrition diet – not in high fat or high fat and high carbohydrate diet – in mice models. These data could be preliminary data to provide a comprehensive study of obesity in pregnancy in poor people, which was caused by carbohydrate overnutrition. The increase in obesity in a poor country could be explained by this study that overnutrition of carbohydrates leads to obesity in the mothers and macrosomia of the fetuses.

5. CONCLUSION

It was concluded that obesity in pregnancy due to carbohydrate overnutrition could have detrimental effects on both mother and developing fetuses.

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REFERENCES

1. Evans SCL, Pearce J and Ellis S., Overweight, obesity, and excessive weight gain in pregnancy as risk factors for adverse pregnancy : A narrative review, *J Hum Nutr Diet*, 2022 ; 35 : 250-264

2. Lin L-h, Lin J, and Yan J-y. , Interactive affection of pre-pregnancy overweight or obesity, excessive gestational weight gain and glucose tolerance test characteristic on adverse pregnancy outcomes among woman with gestational diabetes mellitus, *Front Endocrinol*, 2022, 13; 942271
3. Gomes D, Kries Rv, Delius M, Mansmann U, Nast M, Stubert M et al : Late-pregnancy dysglycemia in obese pregnancies after negative testing for gestational diabetes and risk of future chilhood overweight : An interim analysis from a longitudinal mother-child cohort study, *PLOS Med*, 2018; 15(10) : e1002681
4. Athukorala C, Rumbold AR, Willson KJ, and Crowther CA, The risk of adverse pregnancy outcomes in women who are overweight or obese, *BMC Pregnancy and Childbirth,* 2010; 10:56
5. Owen LA, O'Sullivan EP, Kirwan B, Avalos G, Gaffney G et al. ATLANTIC DIP : The impact of obesity on pregnancy outcome in glucose-tolerant women, *Diabetes Care* 2010; 33:577-579
6. Kruse M, Seki Y, Vuguin PM, Dua XQ, Fiallo A et al : High-fat intake during pregnancy and lactation exacerbates high-fat diet induced complication in male offspring in mice, *Endocrinology*, 2013 : 154(10) : 3565-3576
7. Reynolds RM, Allan KM, Bhattacharya S, McNeill J, Hannaford PC et al. Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring : follow-up of 1 323 275 person years. *BMJ*, 2013; 347
8. Ministry of Health of Indonesian Republic : Indonesian health profile 2016, www.kemkes.go.id
9. Rathnayake KM, Roopasingam T, and Dibley MJ. High carbohydrate diet and physical inactivity with central obesity among premenopausal housewives in Sri Lanka. *BMC Research Notes*, 2014, 7:564
10. Casas R, Barquero SC, and Estruch R : Impact of surgery food comsumption on pregnancy : A Review, *Nutrients*, 2020; 12 : 3574
11. Renault KM, Carlsen EM, Norgaard K, Nilas L, Pryds O et al : Intake of carbohydrate during pregnancy in obese women is associated with fat mass in new born offspring, *Am J Clin Nutr*, 2015; 102 : 1475-81
12. Ehrlich SF, Rosas LG, Ferrara A, King JC, Abrams B et al. Pregnancy glycemia in Mexican-American women without diabetes or gestational diabetes and programing for childhood obesity, *American Journal of Epidemiology,* 2013; Vol 177, No. 8
13. King V, Norman JE, Seckl JR, and Drake AJ. Post-weaning diet determines metabolic risk in mice exposed to overnutrition in early life. *Reproductive Biology and Endocrinology,* 2014; 12:73
14. Zhong Q, Xu J, Long Y, Deng Y, Hu J, Li X, and Qiu X. Interaction of body mass index and hemoglobin concentration on blood pressure among pregnant women in Guangxi China. *BMC Public Health,* 2014; 14:474
15. Choi MJ, Yu J, and Choi J : Maternal pre-pregnancy obesity and gestational diabetes mellitus increase the risk of childhood obesity, *Children*, 2022 ; 9 : 928
16. Bhattacharya S, Campbell DM, Liston WA, and Bhattacharya S. Effect of body mass index on pregnancy outcomes in nulliparous women delivering singleton babies, *BMC Public Health,* 2007, 7:168
17. Busso D, Mascareno L, Salas F, Berkowitz L, Santander N et al. Early onset intrauterine growth restriction in a mouse model of gestational hypercholesterolemia and atherosclerosis, *BioMed Research International*, volume 2014
18. Kang SS, Kurti A, Fair DA, and Fryer JD. Dietary intervention rescues maternal obesity induced behaviour deficits and neurounflammation in offspring, *Journal of Neuroinflammation,* 2014, 11:156

19. Kerssen A, De Valk HW, and Visser GHA : Increased second trimester maternal glucose levels are related to extremely large for gestational age infant in woman with type 1 diabetes, *Diabetes care*, 2007 : 30 : 1069-1074
20. Catalano PM, Mclntyre HD, Cruickshank JK, McCance DR, Dyer AR et al. The hyperglycemia and adverse pregnancy outcome study, *Diabetes Care,* 2012; 35:780-786
21. Tillman EJ, Morgan DA, Rahmouni K, and Swoap SJ : Three months of high frucotose feeding fails to induce excessive weight gain or leptin resintance in mice, *PLOS ONE*, 2014; 9 : e107206
22. Beigy M, Vakili S, Berijani S, Aminizade M, Ahmadi-Dastgerdi M, and Meshkani R :Alternate-day fasting improves fructose-induced resistance insulin in mice, *J Anim Physiol Nutr*, 2013; 97(6) : 1125-31
23. Barrett HL, Nitert MD, D'Emden M, Mclntyre HD and Callaway LK : Validation of triglyceride meter for use in pregnancy, *BMC research Notes,* 2014, 7 : 679
24. Son GH, Kwon JY, Kim YH, and Park YW. : Maternal serum triglycerides as predictive factors for large-for-gestational age newborns in women with gestational diabetes mellitus, *Acta Obstet Gynecol Scand.*, 2010 May ; 89(5):700-4
25. Callegari SB, Resende EA, Barbosa NO, Rodrigues JV, Oliveira EM, and Borges MD : Obesity and cardiometabolic risk factors during pregnancy, *Rev Bras Ginecol Obstet.*, 2014 Oct 3
26. Li G, Kong L, Zhang L, Fan L, Su Y, Rose JC, and Zhang W. Early pregnancy maternal lipid profiles and the risks of gestational diabetes mellitus stratified for body mass index, *Reprod Sci.,* 2014 Nov 12

Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.