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妊娠中期孕妇血糖水平变化与新生儿体质及大脑发育的关系 *

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摘要 目的：探讨妊娠中期孕妇血糖水平变化与新生儿体质及大脑发育的关系。**方法：**2018 年 2 月到 2021 年 1 月选择在本院建档分娩的妊娠中期妊娠期糖尿病(Gestational diabetes，GDM)孕妇 105 例作为研究对象，根据孕妇血糖控制情况进行分组，孕妇血糖控制较好纳入良好组，其他纳入对照组。调查分娩的新生儿体质、大脑发育情况并进行相关性分析。**结果：**在 105 例孕妇中，血糖控制良好 85 例，控制不良 20 例。良好组的孕周、年龄、孕前体重指数、孕次、产次等与对照组对比差异无统计学意义(P>0.05)。良好组新生儿分娩第 3 个月的体重与身长都高于对照组 (P<0.05)。良好组新生儿分娩第 3 个月的 MDI 与 PDI 评分都高于对照组(P<0.05)。在 105 例孕妇中，Spearsman 相关分析显示血糖控制水平与新生儿的体重、身长、智力发育指数(Intelligence Development Index，MDI)评分、精神运动发育指数(Intelligence Development Index，PDI)评分等都存在相关性(P<0.05)。多因素 Logistic 回归分析显示血糖控制水平都为影响新生儿体重、身长、MDI 评分、PDI 评分的危险因素(P<0.05)。**结论：**妊娠中期妊娠期糖尿病孕妇血糖控制水平与新生儿体质、大脑发育存在相关性，血糖控制不佳可导致新生儿体质发育缓慢与智力水平下降。

关键词：妊娠中期；妊娠期糖尿病；血糖控制水平；新生儿体质；大脑发育；相关性

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The Relationship between Pregnant Women's Blood Glucose Level in the Second Trimester of Pregnancy and the Newborn's Physique, Brain Development*

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ABSTRACT Objective: To investigate the relationship between the blood glucose level of pregnant women in the second trimester of pregnancy and the physique, brain development of the newborn. **Methods:** From February 2018 to January 2021, 105 cases of pregnant women with Gestational Diabetes (GDM) in the second trimester of pregnancy who were filed in our hospital were selected as the research objects. The pregnant women were grouped accorded to their blood glucose control status that he pregnant women were better blood glucose control were included the good group, and the others were included into the control group. Investigated the physique and brain development of the newborns during delivery and given correlation analysis. **Results:** There were 85 cases were good blood glucose control and 20 cases were poor control in the 105 cases. The gestational age, age, pre-pregnancy body mass index, pregnancy times, parity, etc. of the good group were not significantly different from those of the control group (P>0.05). The weight and length of newborns in the good group were higher than those in the control group at the third month of delivery (P<0.05). The scores of MDI and PDI of the newborns in the good group were higher than those of the control group at the third month of delivery (P<0.05). In the 105 pregnant women, Spearsman correlation analysis showed that blood glucose control levels were correlated with newborn weight, length, Intelligence Development Index (MDI) score, and psychomotor development index (PDI) score, etc. (P<0.05). Multivariate logistic regression analysis showed that blood glucose control levels were all risk factors affected newborn weight, length, MDI score, and PDI score (P<0.05). **Conclusion:** The blood glucose control level of pregnant women with gestational diabetes in the second trimester are related to the physique and brain development of the newborn. Poor blood sugar control can lead to the slow growth of the newborn's physical development and the decline of intelligence.

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前言

妊娠期糖尿病(Gestational diabetes,GDM)是指在孕期首次发生或发现因糖耐量异常而导致的不同程度的血糖升高[1,2]。该病多发生于孕妇的妊娠中晚期,与机体的胰岛素抵抗和分泌异常等存在相关性[3,4]。该病具有一定的遗传性,并且可提高孕妇妊娠期高血压疾病、胎膜早破、早产、胎儿宫内发育迟滞等发生率,也会增加胎儿发生胎儿缺氧、缺血缺氧性脑病、羊水减少、新生儿窒息的几率, 严重情况下可导致孕妇与围产儿死亡[5-7]。现代研究表明孕妇的生理和代谢状况对胎儿与新生儿的生长发育至关重要,新生儿的体格发育状况与孕妇的血糖水平存在密切相关性[8,9]。孕妇糖脂代谢水平持续异常可导致患儿出现语言理解和表达障碍、生长发育落后、社会交往和适应能力低下、视听和运动功能受损等[10,11]。研究显示:孕早期为满足胎儿生长需要,母体脂肪生成增加,抑制脂肪氧化和分解作用减弱,可导致血脂水平发生变化,易导致分娩巨大儿[12,13]。本文具体探讨了妊娠中期孕妇血糖水平变化与新生儿体质及大脑发育的关系,以明确孕妇血糖控制的价值。现总结报道如下。

1 资料与方法

1.1 研究对象

2018 年 2 月到 2021 年 1 月选择在本院建档分娩的妊娠中期妊娠期糖尿病孕妇 105 例作为研究对象,纳入标准:符合妊娠期糖尿病的诊断标准;单活胎;孕周 12-28 周;孕妇年龄 20-40 岁;自然受孕;临床资料完整;孕妇知情同意本研究;治疗依从性好;本研究得到了医院伦理委员会的批准。排除标准:早产孕妇;存在急慢性感染性、肿瘤、心血管疾病者;孕前糖尿病者;合并精神、智力障碍者;发生流产、死胎等新生儿不能正常产出的样本资料。

1.2 血糖检测

所有患者都给予积极的饮食、运动、药物干预等,持续 5 周,然后检测孕妇的空腹血糖、餐后 2 h 血糖、糖化血红蛋白等指标,当空腹血糖≤ 5.3 mmol/L、餐后 2 h 血糖 ≤ 6.7 mmol/L、糖化血红蛋白≤ 5.5 %、尿酮阴性时,表明孕妇血糖控制较好(良好组),其他纳入对照组。

1.3 观察指标

(1)观察与记录所有孕妇的孕周、年龄、孕前体重指数、孕次、产次等指标。(2)观察与记录新生儿新生儿分娩后 3 个月的体质发育情况,包括体重与身长。(3)采用小儿智能发育量表评定新生儿分娩后 3 个月的大脑发育情况情况,包括智力发育指数(Intelligence Development Index,MDI)与精神运动发育指数(Intelligence Development Index,PDI)两个维度,分数越高,大脑发育发育越好。

1.4 统计方法

选择 SPSS19.00 对数据进行分析,计量资料以均数± 标准差(mean± SD)表示,组间比较采用独立样本 t 检验;计数资料以百分比表示, 对比为卡方 x^2 分析, 相关性分析采用 Spearsman 相关分析,影响因素采用多因素 Logistic 回归分析,检验水准为α=0.05。

2 结果

2.1 血糖控制情况

在 105 例孕妇中,血糖控制良好 85 例,控制不良 20 例。

2.2 一般资料对比

良好组一般资料与对照组对比差异无统计学意义(P>0.05)。见表 1。

表 1 一般资料对比(mean± SD)

Table 1 General information(mean± SD)

Groups	n	Week of pregnancy (weeks)	Age (years)	Pre-pregnancy body mass index(kg/m^2)	Pregnancy (times)	Birth(times)
Good group	85	22.55± 1.95	30.97± 1.76	22.76± 1.59	2.15± 0.13	1.45± 0.11
Control group	20	22.02± 2.09	30.10± 1.11	22.10± 2.14	2.22± 0.12	1.50± 0.07

2.3 新生儿体质对比

良好组新生儿分娩第 3 个月的体重与身长均较对照组显著增加(P<0.05)。见表 2。

表 2 两组新生儿体质对比(mean± SD)

Table 2 Physical comparison between the two groups(mean± SD)

Groups	n	Weight(kg)	Height(cm)
Good group	85	4.89± 0.52	55.22± 2.15
Control group	20	4.40± 0.47*	51.99± 3.03*

Note: Compared with the control group, *P<0.05.

2.4 大脑发育评分对比

良好组新生儿分娩第 3 个月的 MDI 与 PDI 评分都高于组

(P<0.05)。见表 3。

2.5 相关性分析

在 105 例孕妇中，Spearsman 相关分析显示血糖控制水平与新生儿的体重、身长、MDI 评分、PDI 评分等都存在相关性(P<0.05)。见表 4。

表 3 两组新生儿分娩第 3 个月的 MDI 与 PDI 评分对比(分，mean± SD)

Table 3 Comparison of MDI and PDI scores for the third month of neonatal delivery between the two groups (score, mean± SD)

Groups	n	MDI score	PDI score
Good group	85	77.34± 4.94*	81.32± 5.63*
Control group	20	74.89± 4.83	77.35± 5.13

Note: Compared with the control group, *P＜0.05.

表 4 相关性分析(n=105)

Table 4 Correlation analysis(n=105)

Index	Body weight	Height	PDI score	MDI score
r	0.562	0.499	0.613	0.653
P	0.004	0.007	0.001	0.000

2.5 多因素分析

在 105 例孕妇中，多因素 Logistic 回归分析显示血糖控制水平都为影响新生儿体重、身长、MDI 评分、PDI 评分的危险因素(P<0.05)。见表 5。

表 5 影响新生儿体质及大脑发育的多因素 Logistic 回归分析(n=105)

Table 5 Multivariate regression analysis Logistic neonatal physique and brain development (n=105)

Index	β	SE	Wald× 2	OR	95%CI	P
Body weight	0.020	0.039	6.393	1.333	1.109-6.924	0.014
Height	0.075	0.417	5.733	1.873	1.249-5.204	0.019
PDI score	0.178	0.275	9.813	2.033	1.291-7.383	0.000
MDI score	0.702	0.389	10.772	1.620	1.472-8.821	0.000

3 讨论

妊娠期糖尿病是妊娠期常见的并发症，相关研究显示：其发病与孕妇胰岛 β 细胞功能缺陷导致的血糖代谢异常有关[14,15]。相关研究显示：该病具有一定的遗传性，会增加巨大儿与低体重儿的发生几率，也会影响新生儿的大脑发育，为降低新生儿患病的风险性，需要对妊娠期糖尿病孕妇进行干预，对其进行饮食、药物与运动指导，以控制妊娠期糖尿病孕妇的血糖水平[16,17]。但依然有部分妊娠期糖尿病的血糖控制水平存在问题，主要在于每个孕妇的生理状况不一样，家族患病史、不良饮食习惯等也是导致孕妇血糖控制不佳的重要原因[18,19]。同时机体代谢异常和内分泌紊乱会造成妊娠期女性胰岛量增加，进而使得胰岛素水平上升，促使 β 细胞数量增多，可影响孕妇的血糖水平[20]。

在妊娠过程中，由于激素水平及身体状况发生变化，部分孕妇对胰岛素的敏感性下降，也会出现不同程度的胰岛素分泌不足，从而诱导出现妊娠期糖尿病[21,22]。同时孕期会促进孕妇脂肪在肝脏的合成，形成生理性高血脂，从而在血糖紊乱的基础上引起脂质代谢紊乱[23]。本研究显示良好组新生儿分娩第 3 个月的体重与身长都高于对照组(P<0.05)；MDI 与 PDI 评分都高于对照组(P<0.05)，结合相关研究分析：母体高血糖所致的高胰岛素血症的内环境可促进胎儿自身蛋白、脂肪合成，导致其躯干过度发育，从而胎儿易出现出生时肥胖，而随着新生儿的发育，由于其面对的营养环境发生改变，可导致其在新生儿时期发育比较缓慢，导致体重、身长在分娩第 3 个月明显下降[24,25]。

随着孕妇机体内血糖浓度的升高，可使得新生儿的肌张力减弱，胃肠蠕动缓慢，表现胎便排出延迟，逐渐可出现呼吸深度抑制、昏迷等，从而影响新生儿的大脑发育[26,27]。同时血糖水平过高也会干扰血小板粘附和凝血酶原生成时间，过多增加能量、氧和营养物质的供应，增加促进不利于胎儿在母体内的能量代谢和新陈代谢，从而对新生儿的大脑发育产生负面影响[28,29]。另外，本研究 Spearsman 相关分析显示血糖控制水平与新生儿的体重、身长、MDI 评分、PDI 评分等都存在相关性(P<0.05)；多因素 Logistic 回归分析显示血糖控制水平都为影响新生儿体重、身长、MDI 评分、PDI 评分的危险因素(P<0.05)，与上述研究结论相似。因此，在妊娠期孕妇血糖控制措施实施过程中，要积极根据孕妇检测血糖的结果、体重以及孕周变化，合理调整各种治疗与干预措施，必要时给予口服降糖药物二甲双胍、格列本脲甚或胰岛素治疗，尽量使血糖控制在正常范围内或者在正常范围内波动[30,31]。同时妊娠期糖尿病的胰岛素抵抗状态使体内胰升糖素水平升高，可使得胆固醇增多，促进胎儿蛋白质、脂肪的合成代谢增加，也会影响新生儿的智力状况[32,33]。本研究不足之处在于：未进一步对妊娠糖尿病对新生儿的长期预后影响进行分析，将在后续进行深入探讨。

总之，妊娠中期妊娠期糖尿病孕妇血糖控制水平与新生儿体质、大脑发育存在相关性，血糖控制不佳可导致新生儿体质发育缓慢与智力水平下降，因此妊娠早期开始密切关注并及时调控孕妇血糖水平对优生优育具有积极意义。

参考文献(References)

[1] Subiabre M, Silva L, Toledo F, et al. Insulin therapy and its consequences for the mother, foetus, and newborn in gestational diabetes mellitus [J]. Biochim Biophys Acta Mol Basis Dis, 2018, 1864(9): 2949-2956

[2] Tieu J, Mcphee A J, Crowther C A, et al. Screening for gestational diabetes mellitus based on different risk profiles and settings for improving maternal and infant health[J]. Cochrane Database Syst Rev, 2017, 8(8): 7222-7225

[3] Agarwal P, Morriseau T S, Kereliuk S M, et al. Maternal obesity, diabetes during pregnancy and epigenetic mechanisms that influence the developmental origins of cardiometabolic disease in the offspring[J]. Crit Rev Clin Lab Sci, 2018, 55(2): 71-101

[4] Davidson S J, Barrett H L, Price S A, et al. Probiotics for preventing gestational diabetes [J]. Cochrane Database Syst Rev, 2021, 4(12): 9951-9958

[5] Frick A P. Advanced maternal age and adverse pregnancy outcomes [J]. Best Pract Res Clin Obstet Gynaecol, 2021, 70(15): 92-100

[6] Hills A P, Byrne N M, Ahuja K D K, et al. Ketones in Pregnancy: Why Is It Considered Necessary to Avoid Them and What Is the Evidence Behind Their Perceived Risk?[J]. J Clin Med, 2021, 44(1): 280-289

[7] Karaçam Z, Kizilca akaloz D, Demir R. The impact of adolescent pregnancy on maternal and infant health in Turkey: Systematic review and meta-analysis [J]. J Midwifery Womens Health, 2021, 50(4): 102093

[8] Muhammad H F L, Pramono A. The safety and efficacy of supervised exercise on pregnant women with overweight/obesity: A systematic review and meta-analysis of randomized controlled trials [J]. Clinical Obesity, 2021, 11(2): e12428

[9] Rahman M N, Herath M P. Gestational Diabetes Mellitus and Infant Adiposity at Birth: A Systematic Review and Meta-Analysis of Therapeutic Interventions[J]. Clin Obes, 2021, 10(4): 1115-1119

[10] Balsells M, Garcí a-Patterson A, Gich I, et al. Ultrasound-guided compared to conventional treatment in gestational diabetes leads to improved birthweight but more insulin treatment: systematic review and meta-analysis [J]. Acta Obstet Gynecol Scand, 2014, 93(2): 144-151

[11] Berghella V, Caissutti C, Saccone G, et al. The One Step approach for diagnosing gestational diabetes is associated with better perinatal outcomes than the Two Step approach: evidence of randomized clinical trials[J]. Am J Obstet Gynecol, 2019, 220(6): 562-564

[12] Barrett H L, Shpakov A O. Improvement Effect of Metformin on Female and Male Reproduction in Endocrine Pathologies and Its Mechanisms[J]. Diabetes Care, 2021, 14(1): 114-119

[13] Bili E, Karagianni E, Goulis D G, et al. Galanin in pregnancy: Is there an association with birth weight and gestational diabetes?[J]. J Matern Fetal Neonatal Med, 2017, 30(23): 2812-2817

[14] Brannon P M, Taylor C L. Iron Supplementation during Pregnancy and Infancy: Uncertainties and Implications for Research and Policy [J]. Nutrients, 2017, 9(12): 114-119

[15] Carpita B, Muti D. Oxidative Stress, Maternal Diabetes, and Autism Spectrum Disorders [J]. Ultrasound Obstet Gynecol, 2018, 2018(12): 3717215

[16] Champion M L, Harper L M. Gestational Weight Gain: Update on Outcomes and Interventions[J]. Curr Diab Rep, 2020, 20(3): 11-19

[17] Chen Q, Francis E, Hu G, et al. Metabolomic profiling of women with gestational diabetes mellitus and their offspring: Review of metabolomics studies[J]. Int J Mol Sci, 2018, 32(5): 512-523

[18] Davenport M H, Meah V L, Ruchat S M, et al. Impact of prenatal exercise on neonatal and childhood outcomes: a systematic review and meta-analysis[J]. Br J Sports Med, 2018, 52(21): 1386-1396

[19] Dell'osso L, Bgeginski R, Ribeiro P a B, et al. Effects of weekly supervised exercise or physical activity counseling on fasting blood glucose in women diagnosed with gestational diabetes mellitus: A systematic review and meta-analysis of randomized trials [J]. Oxid Med Cell Longev, 2017, 9(11): 1023-1032

[20] Durnwald C. Gestational diabetes: Linking epidemiology, excessive gestational weight gain, adverse pregnancy outcomes, and future metabolic syndrome[J]. Semin Perinatol, 2015, 39(4): 254-258

[21] Farrar D, Simmonds M, Bryant M, et al. Treatments for gestational diabetes: a systematic review and meta-analysis[J]. BMJ Open, 2017, 7(6): e015557

[22] Floriano J F, Willis G, Catapano F, et al. Exosomes Could Offer New Options to Combat the Long-Term Complications Inflicted by Gestational Diabetes Mellitus[J]. Cells, 2020, 9(3): 156-163

[23] Fulcher G R, Peila C, Gazzolo D, et al. Influence of Diabetes during Pregnancy on Human Milk Composition [J]. Diabetes Care, 2020, 12(1): 114-121

[24] Goran M I, Plows J F, Ventura E E. Effects of consuming sugars and alternative sweeteners during pregnancy on maternal and child health: evidence for a secondhand sugar effect[J]. Proc Nutr Soc, 2019, 78(3): 262-271

[25] Groom K M. Antenatal corticosteroids after 34?weeks' gestation: Do we have the evidence?[J]. Semin Fetal Neonatal Med, 2019, 24(3): 189-196

[26] Hartling L, Dryden D M, Guthrie A, et al. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research [J]. Ann Intern Med, 2013, 159(2): 123-129

[27] Iqbal S, Ekmekcioglu C. Maternal and neonatal outcomes related to iron supplementation or iron status: a summary of meta-analyses[J].J Matern Fetal Neonatal Med, 2019, 32(9): 1528-1540

[28] Vargas-Terrones M, Nagpal T S, Barakat R. Impact of exercise during pregnancy on gestational weight gain and birth weight: an overview[J]. Braz J Phys Ther, 2019, 23(2): 164-169

[29] Viecceli C, Remonti L R, Hirakata V N, et al. Weight gain adequacy and pregnancy outcomes in gestational diabetes: a meta-analysis[J]. Obes Rev, 2017, 18(5): 567-580

[30] Zhang L, Wang X H, Zheng X M, et al. Maternal gestational smoking, diabetes, alcohol drinking, pre-pregnancy obesity and the risk of cryptorchidism: a systematic review and meta-analysis of observational studies[J]. J Diabetes, 2015, 10(3): e0119006

[31] Johns E C, Denison F C, Norman J E, et al. Gestational Diabetes Mellitus: Mechanisms, Treatment, and Complications [J]. Trends Endocrinol Metab, 2018, 29(11): 743-754

[32] Khambule L, George J A. The Role of Inflammation in the Development of GDM and the Use of Markers of Inflammation in GDM Screening[J]. BMC Pregnancy Childbirth, 2019, 1134(9): 217-242

[33] Martis R, Crowther C A, Shepherd E, et al. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews[J]. Diabetes Care, 2018, 8(8): 12327-12331