

doi: 10.13241/j.cnki.pmb.2021.19.032

不同孕期 GDM 孕妇 CRP 水平、HbA1c 和维生素 B12 相关性研究*

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摘要 目的: 对不同孕期妊娠期糖尿病(gestational diabetes mellitus, GDM)孕妇的全血 C 反应蛋白(C-reactive protein, CRP)水平、糖化血红蛋白(glycosylated hemoglobin, HbA1c)和血清维生素 B12 水平进行检测,并对其相关性进行分析。**方法:** 以妊娠期孕妇为研究对象,根据 OGTT 试验结果分为对照组和研究组,对照组为健康孕妇,研究组为 GDM 孕妇,对两组中孕期和晚孕期孕妇的全血 CRP、HbA1c 和血清维生素 B12 进行检测。**结果:** 研究组中孕期和晚孕期 GDM 的全血 CRP 和 HbA1c 水平均显著高于对照组($P<0.05$)。与中孕期相比,两组晚孕期全血 CRP 水平均无明显变化($P>0.05$),对照组孕妇全血 HbA1c 水平无明显变化($P>0.05$),而研究组晚孕期全血 HbA1c 水平显著升高($P<0.05$)。与对照组相比,研究组中孕期和晚孕期的血清维生素 B12 水平显著降低($P<0.05$);与中孕期相比,对照组孕妇血清维生素 B12 水平无明显变化($P>0.05$),而研究组晚孕期血清维生素 B12 水平显著降低($P<0.05$)。研究组中孕期和晚孕期 CRP 水平与 HbA1c 呈显著的正相关,与维生素 B12 呈显著的负相关($P<0.05$)。正常孕妇中孕期和晚孕期的 CRP 水平和 HbA1c、维生素 B12 水平均未呈现相关性($P>0.05$)。**结论:** GDM 孕妇中孕期和晚孕期的全血 CRP、HbA1c 和血清维生素 B12 均存在异常,且 CRP 水平与 HbA1c 显著正相关,与维生素 B12 水平显著负相关。

关键词: GDM; 孕期; CRP; HbA1c; 维生素 B12

中图分类号: R714.256 **文献标识码:** A **文章编号:** 1673-6273(2021)19-3756-04

Correlation Study of CRP Level, HbA1c and Vitamin B12 in Pregnant Women with GDM in Different Pregnancy*

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ABSTRACT Objective: The whole blood CRP levels, HbA1c and serum vitamin B12 levels of pregnant women with GDM in different pregnancy periods were detected, and their correlations were analyzed. **Methods:** Taking pregnant women as research subjects, they were divided into control group and study group according to the OGTT test results. The control group was healthy pregnant women and the study group was GDM pregnant women. The whole blood CRP levels, HbA1c and serum vitamin B12 of pregnant women in the second and third trimesters of the two groups were tested. **Results:** The whole blood CRP and HbA1c levels of GDM in the second and third trimesters of the study group were significantly higher than those of the control group ($P<0.05$). Compared with the second trimester, there was no significant change in the whole blood CRP level of the two groups in the third trimester ($P>0.05$), the whole blood HbA1c level of pregnant women in the control group did not change significantly ($P>0.05$), while the whole blood HbA1c level of the study group was significantly increased in the third trimester ($P<0.05$). Compared with the control group, the serum vitamin B12 levels of the study group during the second and third trimesters were significantly reduced ($P<0.05$); compared with the second trimester, the serum vitamin B12 levels of pregnant women in the control group did not change significantly ($P>0.05$), while serum vitamin B12 level in the third trimester of the study group was significantly reduced ($P<0.05$). The CRP levels in the second and third trimesters of the study group were significantly positively correlated with HbA1c, and significantly negatively correlated with vitamin B12 ($P<0.05$). There was no correlation between CRP levels and HbA1c and vitamin B12 levels in normal pregnant women during the second and third trimesters ($P>0.05$). **Conclusion:** The whole blood CRP, HbA1c and serum vitamin B12 of GDM pregnant women were abnormal in the second and third trimesters, and the CRP level was significantly positively correlated with HbA1c, and significantly negatively correlated with the vitamin B12 level.

Key words: GDM; Pregnancy; CRP; HbA1c; Vitamin B12

Chinese Library Classification(CLC): R714.256 **Document code:** A

Article ID: 1673-6273(2021)19-3756-04

* 基金项目:陕西省卫生计生委科研基金项目(2016D056)

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(收稿日期:2020-11-30 接受日期:2020-12-26)

前言

妊娠期糖尿病(gestational diabetes mellitus, GDM)是常见的妊娠合并症^[1],其妊娠过程中可能出现早产、产后大出血、流产等严重并发症^[2-4],也会对胎儿造成严重影响,如胎儿器官发育迟滞、体重过大、畸形、胎死宫内等^[5-7],对孕产妇和胎儿均有严重的危害,因此尽早诊断 GDM,对患者进行及时有效的干预,对母婴均有重要意义。目前糖尿病诊断的金标准是葡萄糖耐量试验,但该方法检测操作复杂、多次抽血,患者依从性低,因此有必要寻找一种方便、安全有效的检测手段进行 GDM 的诊断^[8-10]。

CRP 是机体处于急性反应过程中最敏感的炎性因子,与糖代谢紊乱发生、进展过程有关,可干扰胰岛素在体内的传导^[11-13]。HbA1c 能够体现患者在过去一段时间内的血糖控制的平均水平,某次血糖的升高或者降低不会对 HbA1c 造成影响^[14-16]。因此对 GDM 患者进行 HbA1c 检测能较好的掌握其近期血糖控制的情况。有研究表明,HbA1c 对 GDM 患者的治疗、终止妊娠和预测围产儿结局均有重要的指导意义,同时也是糖尿病慢性

并发症的一个危险因素^[17-19]。维生素 B12 又叫钴胺素,是同型半胱氨酸(Hcy)代谢的辅助因子,可将 Hcy 转化为蛋氨酸,Hcy 与胰岛素敏感性下降有关。维生素 B12 缺乏会导致 Hcy 水平增加。糖尿病患者可能存在维生素 B12 缺乏,有报道表明,二甲双胍的长期使用能引起维生素 B12 的缺乏和 Hcy 的升高,且与剂量有关^[20,21]。

因此本研究对不同孕期 GDM 孕妇的 CRP 水平、HbA1c 和维生素 B12 水平进行检测,并对其相关性进行分析,具体如下。

1 资料与方法

1.1 基本资料

以 2018 年 1 月~2020 年 2 月就诊于我院的妊娠期孕妇为研究对象,根据 OGTT 试验结果分为对照组和研究组,对照组(50 例)为健康孕妇,研究组(50 例)为 GDM 孕妇,一般资料见表 1 所示,两组患者基本信息如年龄、孕期、孕前 BMI 等经分析无统计学意义($P>0.05$),具有可比性。患者及家属均充分了解研究内容并签署知情同意书,本研究已获得医院伦理委员会的准许。

表 1 基本资料比较
Table 1 Comparison of basic data

Groups	Age(years)		Second trimester		Third trimester		BMI before pregnancy (Kg/m ²)	Primipara (case)	Maternal (case)
	Age range	Average age	Number of cases	Gestational week	Number of cases	Gestational week			
Control group(n=50)	24~39	30.3±6.8	35	26.33±0.95	15	39.18±0.81	22.51±2.40	30	20
Study group (n=50)	23~40	31.1±5.9	33	26.11±0.74	17	38.95±0.85	23.17±3.28	31	19

1.2 诊断标准

依据《妊娠合并糖尿病诊治指南(2014)》等制定诊断标准^[22],于妊娠 24~28 w 进行口服葡萄糖耐量试验,检测前禁食 8~14 h,分别于空腹、服糖后 1 h 和 2 h 检测血糖水平。临界值分别为:空腹血糖 ≥ 5.1 mmol/L,服糖后 1 h 血糖 ≥ 10.0 mmol/L,服糖后 2 h 血糖 ≥ 8.5 mmol/L,若有任何一项符合,即诊断为 GDM。

1.3 纳入与排除标准

纳入标准:(1)符合 GDM 诊断标准;(2)入组前 3 个月内均未服用微量元素类药物;(3)饮食习惯正常;(4)认知功能正常,依从性好,能配合检验者。

排除标准:(1)合并高血压等疾病妊娠;(2)合并心、肝、肾等脏器功能不全者;(3)既往有血液、免疫、内分泌、心血管系统等疾病者;(4)伴有精神系统障碍性疾病。

1.4 研究方法

对两组研究对象中孕期和晚孕期孕妇全血 CRP、HbA1c 和血清维生素 B12 进行检测。于清晨抽取空腹肘静脉血 5 mL,分成 2 份,1 份室温静置 20 min,后以 3000 r/min 离心 10 min,取上层血清储存待测,储存温度为 -20℃,以化学发光免疫分析法检测维生素 B12,试剂盒均购自罗氏公司。1 份加乙二胺四乙酸二钾(EDTA-k2)抗凝(血常规管),采用免疫层析法检测

CRP,检测仪器为艾瑞德快速免疫干式分析仪,试剂盒为该公司的配套试剂。采用高效液相色谱法检测 HbA1c,仪器为美国伯乐(Bio-Rad)公司生产的 VARIANT II Turbo(VIIT)数字化血红蛋白 A1C 测定仪,试剂也由该公司提供。分析两组研究对象不同孕期 CRP、HbA1c 和血清维生素 B12 变化情况。判断标准为:CRP >5 mg/L 为异常,HbA1c $>6\%$ 为异常,维生素 B12 正常范围为 189~883 pg/mL, <100 pg/mL 为缺乏。

1.5 数据处理

以 SPSS 19.0 对数据进行分析,计量资料以 $\bar{x}\pm s$ 表示,使用 t 检验,计数资料采用率(%)表示,计量资料使用 χ^2 检验, $P<0.05$ 为具有统计学意义。

2 结果

2.1 不同孕期 GDM 全血 CRP 和 HbA1c 水平

对两组中孕期和晚孕期孕妇的全血 CRP 水平进行检测,结果见表 2 所示,研究组中孕期和晚孕期 GDM 的全血 CRP 和 HbA1c 水平均显著高于对照组($P<0.05$)。与中孕期相比,两组晚孕期全血 CRP 水平无明显变化($P>0.05$),对照组孕妇全血 HbA1c 水平无明显变化($P>0.05$),而研究组晚孕期全血 HbA1c 水平显著升高($P<0.05$)。

2.2 不同孕期 GDM 血清维生素 B12 水平比较

对两组中孕期和晚孕期孕妇的血清维生素 B12 水平进行检测,结果见表 3,与对照组相比,研究组中孕期和晚孕期的血清维生素 B12 水平显著降低($P<0.05$);与中孕期相比,对照组

孕妇血清维生素 B12 水平无明显变化($P>0.05$),而研究组晚孕期血清维生素 B12 水平显著降低($P<0.05$)。

表 2 不同孕期 GDM 全血 CRP 和 HbA1c 水平

Table 2 The levels of whole blood CRP and serum vitamin B12 of pregnant women with GDM in different pregnancy

Groups	Second trimester			Third trimester		
	n	CRP (mg/L)	HbA1c(%)	n	CRP (mg/L)	HbA1c(%)
Control group (n=50)	35	2.41±0.51	4.97±0.24	15	2.45±0.45	5.07±0.37
Study group (n=50)	33	4.30±0.81*	6.12±0.28*	17	4.67±0.94*	6.98±0.52*

Note: a compared with the control group, $P<0.05$.

2.3 不同孕期 GDM 患者 CRP 与 HbA1c 和维生素 B12 相关性研究

对不同孕期 GDM 患者 CRP 与 HbA1c 和维生素 B12 相

关性进行分析,结果见表 4 所示,研究组中孕期和晚孕期 CRP 水平与 HbA1c 呈显著的正相关,与维生素 B12 呈显著的负相关($P<0.05$)。

表 3 不同孕期 GDM 血清维生素 B12 水平比较

Table 3 Comparison of serum vitamin B12 levels in GDM during different pregnancy

Groups	Second trimester		Third trimester	
	n	Vitamin B12(pg/mL)	n	Vitamin B12(pg/mL)
Control group(n=50)	35	247.98±45.57	15	252.38±54.12
Study group (n=50)	33	148.27±38.14*	17	117.35±33.74**

Note: * compared with the control group, $P<0.05$; # compared with the second trimester, $P<0.05$.

表 4 不同孕期 GDM 患者 CRP 与 HbA1c 和维生素 B12 相关性

Table 4 Correlation between CRP and HbA1c and vitamin B12 in GDM patients in different pregnancy

Index	Groups	Second trimester		Third trimester	
		r	P	r	P
HbA1c	Control group	0.18	0.20	0.03	0.71
	Study group	0.36	<0.05	0.57	<0.05
Vitamin B12	Control group	0.20	0.14	0.16	0.28
	Study group	-0.46	<0.05	-0.59	<0.05

3 讨论

GDM 是指妊娠期间由糖耐量受损引起的内分泌疾病,我国 GDM 的发病率为 1%~5%,且不断升高,是最常见的妊娠合并症之一^[23]。其发病机制类似 II 型糖尿病,一般认为与遗传、炎症、肥胖、胰岛素抵抗以及胰岛 β 细胞功能缺陷等因素有关^[24]。常出现于妊娠中后期,这段时期孕妇体内抗胰岛素物质增加,使胰岛素对葡萄糖摄取与利用的促进作用降低,引起胰岛素代偿性分泌过多,但依旧难以弥补胰岛素抵抗的增加,使机体难以维持正常血糖代谢,最终导致血糖升高。GDM 可增加产妇产后流产、早产、感染等的发生率,再次妊娠时的复发率可达 33%~69%,一般可在产后恢复正常,但是依旧有 17%~63% 患者于产后发展为 II 型糖尿病,且 GDM 患者远期心血管系统疾病的发生率较高,因此尽早发现 GDM,以便于有效控制患者血糖,对母婴的健康均有重要意义^[25]。

CRP 是常见的炎症因子,其水平的升高与胰岛素抵抗密切相关,而高血糖对 CRP 的分泌有促进作用,可进一步加重 GDM 的进展^[26]。糖化血红蛋白(HbA1c)的合成过程缓慢且相对不可逆,其合成速率与血糖浓度呈正相关,能反映 3 个月内的平均血糖水平,研究表明,HbA1c 水平和慢性糖尿病并发症的产生密切相关^[27,28]。维生素 B12 是人体不可缺少的营养物质,也是 Hcy 代谢的辅助因子,Hcy 的升高与胰岛素抵抗和胰岛素敏感性降低密切相关。妊娠期间机体对维生素 B12 的需求量及消耗量极大的增加,维生素 B12 的缺乏会引起 Hcy 升高。维生素 B12 也是胚胎发育中必不可少的元素,人体自身不能合成,若妊娠期间缺乏维生素 B12,会增加胎儿缺陷的风险^[29-31]。本研究对 GDM 孕妇和健康孕期中孕期和晚孕期的全血 CRP 和 HbA1c 和血清维生素 B12 水平进行检测,结果表明,与对照组相比,研究组中孕期和晚孕期 GDM 的全血 CRP 和 HbA1c 水平平均显著升高。与中孕期相比,两组晚孕期全血 CRP 水平均无

明显变化,对照组孕妇全血 HbA1c 水平无明显变化,而研究组晚孕期全血 HbA1c 水平显著升高,与凌思思^[32]等学者的研究类似,探讨妊娠早期孕妇炎症因子水平与发生妊娠期糖尿病(GDM)的相关性,选择妊娠中期(24~28 周)确诊为 GDM 的孕妇,同期糖耐量正常孕妇为对照组,结果显示,GDM 组 CRP 显著高于对照组孕妇的妊娠早期;与对照组相比,研究组中孕期和晚孕期的血清维生素 B12 水平显著降低;与中孕期相比,对照组孕妇血清维生素 B12 水平无明显变化,而研究组晚孕期血清维生素 B12 水平显著降低。本研究对不同孕期 GDM 患者和健康孕妇的 CRP 与 HbA1c 和维生素 B12 相关性进行分析,结果研究组中孕期和晚孕期 CRP 水平与 HbA1c 呈显著的正相关,与维生素 B12 呈显著的负相关,而正常孕妇中孕期和晚孕期的 CRP 水平和 HbA1c、维生素 B12 水平均未呈现相关性。闫学平^[33]等学者对 GDM 患者血清 HbA1c 与 CRP 的关系进行了研究,选择了 GDM 孕妇和正常孕妇,GDM 组患者血清 HbA1c 和 CRP 水平均显著高于正常组,GDM 患者血清 HbA1c 和 CRP 水平呈显著正相关关系;谢琴^[34]的研究也与本研究类似,探究妊娠期糖尿病与 Hcy、叶酸(FA)、维生素 B12 及血脂的相关性研究,GDM 患者为实验组,正常孕妇为对照组,实验组 Hcy、TG、LDL 血糖水平高于对照组,FA、维生素 B12、HDL 低于对照组,GDM 患者 Hcy 水平与 FA、维生素 B12、HDL 呈负相关,与 TG、LDL 呈正相关。但是临床关于 GDM 患者的 CRP 与维生素 B12 水平的关系尚没有报道。因此。后续要继续研究二者之间的关系。

综上所述,GDM 孕妇中孕期和晚孕期的全血 CRP、HbA1c 和血清维生素 B12 均存在异常,且 CRP 水平与 HbA1c 显著正相关,与维生素 B12 水平显著负相关,应尽早对糖尿病妊娠患者进行血糖控制、抗炎、补充维生素 B12 等治疗,促进血糖恢复正常水平。

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