

## 妊娠期高血糖孕妇孕晚期初乳收集的安全性及 产后母乳喂养评价

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**【摘要】** 目的 初步探索妊娠期高血糖孕妇孕晚期初乳收集的安全性,并进行产后母乳喂养评价。方法 采用随机对照分组法,前瞻性地将2022年7—11月在复旦大学附属妇产科医院产检的妊娠期高血糖孕妇随机分为孕晚期初乳收集组( $n=52$ )及对照组( $n=55$ )。采用 $t$ 检验、 $\chi^2$ 检验、Fisher精确概率法及秩和检验对数据进行统计学分析,比较两组的分娩结局、新生儿结局及产后母乳喂养情况。结果 两组妊娠期高血糖孕妇的分娩孕周、分娩方式、产后42天及产后4个月母乳喂养率差异均无统计学意义,新生儿出生后1 min及5 min Apgar评分、新生儿入院率差异均无统计学意义。孕晚期初乳收集组孕妇产后首次补充喂养配方奶的比例及产后3天泌乳延迟率显著低于对照组( $P$ 均 $<0.05$ ),其产后24 h、产后3天纯母乳喂养率( $P$ 均 $<0.05$ )显著高于对照组。结论 妊娠期高血糖孕妇孕晚期进行初乳收集是安全的,并且能够降低产后配方奶补充喂养率,提高产后24 h及产后3天的纯母乳喂养率。

**【关键词】** 妊娠期高血糖; 分娩结局; 母乳喂养; 初乳收集

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## Safety of colostrum collection in the third trimester and evaluation of postpartum breastfeeding in pregnant women with hyperglycemia during pregnancy

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**【Abstract】** **Objective** To preliminarily explore the safety of collecting colostrum in the third trimester, and to evaluate postpartum breastfeeding in pregnant women with hyperglycemia during pregnancy. **Methods** Pregnant women with hyperglycemia during pregnancy who had prenatal examinations in Obstetrics and Gynecology Hospital, Fudan University from Jul to Nov 2022 were prospectively divided into the colostrum collection group ( $n=52$ ) in the third trimester and the control group ( $n=55$ ) by randomized controlled grouping method. The  $t$ -test,  $\chi^2$  test, Fisher's exact probability method and rank sum test were used for statistical analysis of the data to compare the delivery outcomes, neonatal outcomes and postpartum breastfeeding status between the two groups. **Results** There were no significant differences in the gestational weeks at delivery, delivery methods, breastfeeding rates at 42 days postpartum and 4 months postpartum between the two groups of pregnant women with hyperglycemia

during pregnancy. There were also no significant differences in the Apgar scores at 1 minute and 5 minutes after birth and the neonatal hospitalization rate. The proportion of formula milk as the first supplementary feeding after delivery and the delayed lactation rate at 3 days postpartum in the colostrum collection group were significantly lower than those in the control group ( $P < 0.05$ ). The exclusive breastfeeding rates at 24 hours postpartum and 3 days postpartum in the colostrum collection group were significantly higher than those in the control group ( $P < 0.05$ ). **Conclusion** Collecting colostrum in the third trimester among pregnant women with hyperglycemia during pregnancy is safe, and it can reduce the rate of supplementary feeding with formula milk after delivery, and increase the exclusive breastfeeding rates at 24 hours postpartum and 3 days postpartum.

**【Key words】** hyperglycemia during pregnancy; delivery outcome; breastfeeding; colostrum collection

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妊娠期高血糖包括孕前糖尿病合并妊娠、糖尿病前期和妊娠期糖尿病(gestational diabetes mellitus, GDM)<sup>[1]</sup>。妊娠期高血糖发病率不断上升,国际糖尿病联盟2021年发布的第10版全球糖尿病地图显示,全球有2 100万活产儿受到妊娠期高血糖的影响,我国妊娠期高血糖患病率为8.6%,其中妊娠期间受高血糖影响的活产儿超过100万<sup>[2]</sup>。

母乳是婴儿最理想的食物,母乳喂养不仅能够降低妊娠期高血糖产妇的体重及2型糖尿病发生风险,还能够稳定新生儿血糖水平,减少新生儿代谢性疾病的发生风险<sup>[3-4]</sup>。妊娠期高血糖产妇的母乳喂养情况却不乐观,妊娠期高血糖产妇母乳喂养率低于正常产妇<sup>[5]</sup>。国外妊娠期高血糖产妇出院时母乳喂养率低于正常产妇(62.2% vs. 75.4%)<sup>[6]</sup>,国内妊娠期高血糖产妇产后2周母乳喂养率为68.1%,产后6个月降至28.7%<sup>[7]</sup>。我国妊娠期高血糖产妇母乳喂养情况类似,吴李楠等<sup>[8]</sup>的调查显示妊娠期高血糖产妇出院前纯母乳喂养率仅为34.45%,远低于中国儿童发展纲要(2021—2030年)中提出的将0~6个月婴儿的纯母乳喂养率提升至50%的目标。

孕晚期收集和存储初乳,利于提升妊娠期高血糖产妇产后母乳喂养成功率,促进母婴健康<sup>[9]</sup>。然而,孕晚期刺激乳房和催产素释放之间存在一定联系,临床上对其可能诱发早产或流产也有所担心<sup>[10]</sup>。目前国内尚缺乏妊娠期高血糖孕妇孕晚期初乳收集的相关研究。本研究采用前瞻性随机对照的方法探索妊娠期高血糖孕妇孕晚期初乳收集的安全性,并进行产后母乳喂养情况评价。

## 资料和方法

**研究对象** 2022年7—11月于复旦大学附属妇产科医院杨浦院区产科门诊招募妊娠期高血糖孕妇入组。纳入标准:(1)孕34~36<sup>+</sup>6周;(2)诊断为妊娠期高血糖;(3)初产妇;(4)单胎妊娠;(5)分娩后计划母乳喂养。排除标准:(1)孕期出血史;(2)前置胎盘;(3)子宫外科手术史;(4)确诊或疑似胎儿异常;(5)严重的妊娠合并症及内科合并症;(6)精神障碍。本研究经我院伦理委员会批准(批准号:2020-163),所有入组孕妇均签署知情同意书。

### 研究方法

**相关定义** 妊娠期高血糖诊断标准参考中华医学会围产医学分会2022年发布的妊娠期高血糖诊治指南<sup>[1]</sup>。孕晚期初乳收集是指在孕晚期用手按压乳房进行初乳收集及存储<sup>[9]</sup>。

**试验组**:对符合纳排标准的妊娠期高血糖孕妇进行20 min无刺激胎心监护检查(nonstress test, NST),NST结果为有反应性且无明显宫缩则纳入试验组。在NST监护下,课题组成员协助孕妇进行初乳收集,同时向其宣教:若自觉宫缩或胎心监护见规律宫缩则立即停止初乳收集。孕妇主诉头昏、出冷汗、低血糖等不适时予以监测血糖水平。孕37周开始,孕妇于家中每天2次收集初乳,每次不超过10 min,直到入院分娩为止。收集过程中若有任何不适(子宫收缩、胎动异常、阴道出血、低血糖等不适)应停止初乳收集并及时联系研究小组。本研究中孕妇自行收集初乳过程中未发生异常情况。

采用自行设计的乳汁收集器将乳汁收集于一次性储奶袋中,注明收集时间、孕妇信息,置于冰箱储存。对照组:孕妇接受正常产检外,不提供孕晚期初乳收集相关的信息。

根据我院新生儿科血糖监测标准,于分娩后0、1、2、4、6 h对新生儿进行血糖监测:血糖 $<3.3$  mmol/L予以补充母乳或配方奶喂养,血糖 $<3.0$  mmol/L予以糖水补充喂养。初乳收集阶段,对研究对象、干预措施的执行者不实行盲法;统计分析阶段,对统计人员实行盲法。

**观察指标** 主要结局指标:分娩孕周和新生儿入院率。次要结局指标:分娩方式,新生儿出生后1 min和5 min Apgar评分,产后24 h、3天和4个月纯母乳喂养率,首次补充喂养情况,产后3天泌乳延迟率。

**样本量计算及分组方法** 选取符合纳入标准的妊娠期高血糖孕妇20例(试验组和对照组各10例)进行预实验,根据预实验结果,确定样本量。预实验中,试验组和对照组产后4个月纯母乳喂养率分别为60%和40%( $P_1=0.6$ 、 $P_2=0.4$ ),取 $\alpha=0.05$ , $\beta=0.10$ ,计算出样本量为51例,考虑10%的样本流失率,最终确定样本量为58例。样本量计算公式:

$$n_1 = n_2 = \frac{\left[ \mu_{d2} \sqrt{2\bar{P} - (1 - \bar{P})} + u_{\beta} \sqrt{P_1(1 - P_1) + P_2(1 - P_2)} \right]^2}{(P_1 - P_2)^2}$$

根据纳排标准,纳入116例妊娠期高血糖孕妇,每组58例。研究对象签署知情同意后随机抽取信封(1为对照组、2为试验组),根据信封内的编号进行分组。试验组3人因担心安全性中途退出,1人未在本院分娩予以排除、2人拒接随访电话予以排除,最终纳入52人。对照组1人分娩后新生儿转院、2人拒接随访电话予以排除,最终纳入55人。

**质量控制** 本课题组成员均为国际认证泌乳顾问。课题组成员统一培训,培训内容包括孕晚期初乳收集方法、纯母乳喂养率的调查方法、泌乳延迟的判断标准等。

**统计学分析** 采用SPSS 22.0软件对数据进行统计学分析。计数资料用 $n(\%)$ 表示,采用 $\chi^2$ 检验或Fisher精确概率法进行比较。正态分布的计量资料以 $\bar{x} \pm s$ 表示,组间比较采用 $t$ 检验,两组间比较采用方差分析。 $P < 0.05$ 为差异有统计学意义。

## 结 果

**两组妊娠期高血糖孕妇的一般情况** 两组妊娠期高血糖孕妇年龄、孕前BMI、文化程度、家庭收入、婚姻状况、生育津贴、分娩镇痛及新生儿体重等一般情况差异无统计学意义(表1),两组新生儿性别差异有统计学意义( $P=0.043$ )。

表1 两组妊娠期高血糖孕妇及新生儿一般情况的比较

Tab 1 Comparison of general information of pregnant women with hyperglycemia during pregnancy and

newborns between the two groups [ $\bar{x} \pm s$  or  $n(\%)$ ]

Items	Colostrum collection group ( $n=52$ )	Control group ( $n=55$ )	$t/\chi^2$	$P$
Age (y)	32.15 $\pm$ 3.369	32.95 $\pm$ 4.089	1.322	0.253
Pre-pregnancy BMI	23.147 $\pm$ 3.791	22.760 $\pm$ 3.127	1.939	0.167
Educational level			1.427	0.490
Junior college and below	5 (9.6)	9 (16.4)		
Bachelor	40 (76.9)	37 (67.3)		
Master's degree or above	7 (13.5)	9 (16.4)		
Native place			2.732	0.098
Shanghai	21 (40.4)	31 (56.4)		
Other	31 (59.6)	24 (46.3)		
Monthly household income (Yuan)			0.101	0.951
$<10\ 000$	4 (7.7)	5 (9.1)		
$10\ 000-30\ 000$	26 (50)	28 (50.9)		
$>30\ 000$	22 (42.3)	22 (40.0)		
Marital status			1.068	0.301
Married	51 (98.1)	55 (100)		
Unmarried	1 (1.9)	0 (0)		
Other	0 (0)	0 (0)		
Maternity insurance and allowance			0.213	0.645
No	6 (11.5)	8 (14.5)		
Yes	46 (88.5)	47 (85.5)		
Labor analgesia			1.226	0.268
Yes	20 (38.5)	27 (49.1)		
No	32 (61.5)	28 (50.9)		
Gender of newborn			4.079	<b>0.043</b>
Male	22 (42.3)	21 (61.8)		
Female	30 (57.7)	34 (38.2)		
Birth weight (g)	3 177.12 $\pm$ 442.80	3 260.55 $\pm$ 437.49	0.553	0.499

**试验组孕晚期初乳收集情况** 试验组孕妇平均初乳收集量为 3.74 mL,最大初乳收集量为 48 mL。首次初乳收集量为 0~12 mL,平均为 0.76 mL。初乳收集次数 2~36 次。

两组妊娠期高血糖孕妇的分娩结局比较 与

对照组相比,试验组孕妇分娩方式、分娩孕周、新生儿出生后 1 min 及 5 min Apgar 评分差异均无统计学意义(表 2),说明妊娠期高血糖孕妇孕晚期收集初乳是安全的。

表 2 两组分娩结局的比较

Tab 2 Comparison of delivery outcome between the two groups

[ $\bar{x} \pm s$  or  $n(\%)$ ]

Items	Colostrum collection group ( $n=52$ )	Control group ( $n=55$ )	$t/\chi^2$	$P$
Mode of delivery				
Vaginal delivery	36 (69.2)	33 (60.0)	0.994	0.319
Cesarean section	16 (30.8)	22 (40.0)		
Gestational age of delivery (wk)	39.178 $\pm$ 0.844	39.296 $\pm$ 0.912	0.498	0.482
Apgar score			-1.00	0.320
1 min	8.98 $\pm$ 0.14	9.00 $\pm$ 0.00	4.404	0.306
5 min	9.00 $\pm$ 0.00	9.00 $\pm$ 0.00		
Newborns admitted to hospital			0.157	0.692
Admission	8 (15.4)	7 (12.7)		
Unadmitted	44 (84.6)	48 (87.3)		

试验组产后首次配方奶补充喂养率及产后 3 天泌乳延迟率均低于对照组(表 3)。试验组产后 24 h 及产后 3 天的纯母乳喂养率高于对照组( $P$  均 <

0.05),但是两组产后 42 天及产后 4 个月纯母乳喂养率差异无统计学意义(表 4)。

表 3 两组产后首次补充喂养方式及产后 3 天泌乳延迟情况的比较

Tab 3 Comparison of the first supplementary feeding method and delayed lactation 3 days after delivery between the two groups

[ $n(\%)$ ]

Items	Colostrum collection group ( $n=52$ )	Control group ( $n=55$ )	$\chi^2$	$P$
Newborn supplementary feeding			30.401	<0.001
No supplementary feeding	17 (32.7)	6 (10.9)		
Breast milk supplementary feeding	14 (26.9)	0 (0)		
Formula milk supplementary feeding	21 (40.4)	49 (89.1)		
Delayed lactation 3 days after delivery			0.817	0.366
Yes	7 (13.5)	44 (80.0)		
No	45 (86.5)	11 (20.0)		

表 4 两组产后不同时间段母乳喂养情况比较

Tab 4 Comparison of breastfeeding status between the two groups at different postpartum periods

[ $n(\%)$ ]

Item	Colostrum collection group ( $n=52$ )			Control group ( $n=55$ )			$\chi^2$	$P$
	Breast feeding	Mixed feeding	Artificial feeding	Breast feeding	Mixed feeding	Artificial feeding		
24 h after delivery	17 (32.7)	34 (65.4)	1 (1.9)	6 (11.5)	46 (88.5)	0 (0)	8.06	0.016
3 d after delivery	24 (46.2)	27 (51.9)	1 (1.9)	12 (23.1)	40 (76.9)	0 (0)	7.52	0.018
42 d after delivery	26 (50.0)	25 (48.1)	1 (1.9)	22 (42.3)	29 (55.8)	1 (1.9)	0.63	0.743
4 mo after delivery	23 (44.2)	28 (53.8)	1 (1.9)	23 (44.2)	27 (51.9)	2 (3.8)	0.35	0.884

## 讨 论

妊娠期高血糖孕妇孕晚期初乳收集的安全性

在保证孕妇和胎儿安全的前提下,孕晚期初乳收集才能成为促进妊娠期高血糖孕妇母乳喂养的可行性措施。本研究的主要结局指标为分娩孕周及新生儿入院率。试验组 2 名孕妇在 NST 监护下首次

收集初乳时出现无痛性子宫收缩,后续自行收集初乳过程中未出现自觉性子宫收缩,且两组产妇分娩孕周并无显著性差异。文献曾报道相似情况:孕晚期初乳收集过程中部分孕妇出现短暂子宫收缩,但并未影响胎儿健康。目前尚未发现孕晚期初乳收集与不良安全结局相关的证据,包括子宫过度收缩或提前分娩,孕晚期乳房按摩组与对照组在新生儿入院率、分娩孕周、新生儿出生体重、分娩方式之间的差异均无统计学意义<sup>[11]</sup>。研究显示女性在哺乳期妊娠,妊娠过程中继续母乳喂养不会增加流产和早产风险<sup>[12-13]</sup>。Forster等<sup>[9]</sup>的研究结果表明孕晚期初乳收集不会诱发宫缩。关于妊娠合并糖尿病孕妇孕晚期初乳收集的预实验结果表明,孕晚期初乳收集增加了新生儿低血糖的风险<sup>[14]</sup>。但该研究并未说明新生儿血糖测量与喂养的关系,也未描述新生儿出生后的血糖测量时间。Forster等<sup>[9]</sup>的研究结果表明,妊娠期高血糖孕妇孕晚期初乳收集不会导致新生儿低血糖,建议妊娠期高血糖孕妇孕晚期初乳收集。本研究试验组新生儿出生后未出现低血糖。2021年昆士兰母乳喂养指南中提及,应向妊娠期高血糖孕妇提供孕晚期初乳收集的相关信息<sup>[15]</sup>。

**妊娠期高血糖孕妇孕晚期初乳收集的可行性** 妊娠中期乳腺上皮增生加快,在催乳素的作用下腺泡开始分泌,形成初乳。妊娠后期乳腺分泌活动明显增强,腺泡腔内充满大量初乳,部分孕妇此时乳头会排出淡黄色黏稠分泌物。孕晚期初乳收集将储存在乳腺腺泡腔内的乳汁排出,同时能够增加乳腺组织中催乳素受体的浓度<sup>[16]</sup>,缩短产后泌乳Ⅱ期时间,增加产后泌乳量<sup>[11,17]</sup>。本研究也证明了妊娠期高血糖孕妇孕晚期初乳收集的可行性,试验组孕妇产前初乳收集量最多为48 mL,完全能够满足产后早期新生儿的喂养需求。

**妊娠期高血糖孕妇孕晚期初乳收集的可接受性** 国外对孕晚期进行初乳收集孕妇的质性访谈结果表明:虽然担忧孕晚期初乳收集可能诱发子宫收缩进而导致提前分娩,但这种担忧通常会随着预产期的临近而消失。本研究中试验组孕妇产前平均初乳收集次数大于12次,说明妊娠期高血糖孕妇可接受孕晚期初乳收集。国外也有孕妇表示孕晚期初乳收集对增加母乳喂养的信心和准备程度有帮助,且会在以后的妊娠中再次进行孕晚期初乳收集<sup>[14]</sup>。另一方面,妊娠期高血糖孕妇表示血糖水平

监测、胰岛素使用及孕期膳食管理已经占用很多时间,再进行初乳收集的难度较大,特别是孕期继续工作的女性<sup>[18]</sup>。初乳收集手法的专业性、乳房按摩过程中的不适感及害羞尴尬的情绪均可能导致妊娠期高血糖孕妇拒绝孕晚期初乳收集<sup>[19]</sup>,因此妊娠期高血糖孕妇孕期是否需要初乳收集,应根据患者自身妊娠情况及其对初乳收集的接受度进行综合评估。

**妊娠期高血糖孕妇孕晚期初乳收集能够提升产后早期母乳喂养率** 妊娠期高血糖孕妇孕早期胎儿暴露于高胰岛素环境中,分娩后胎儿源自母体的葡萄糖供应中断,持续的高胰岛素血症易导致新生儿发生低血糖<sup>[20]</sup>。若出生后无法立即获得充足的初乳,新生儿喂养不足有发生低血糖风险或已经发生低血糖时,只能添加配方奶、口服或静脉使用葡萄糖溶液纠正低血糖,进而增加新生儿添加配方奶及母婴分离概率。妊娠期母体高血糖的新生儿产后添加配方奶而过早接触牛乳蛋白,会增加新生儿远期1型和2型糖尿病的发病风险<sup>[21-22]</sup>。因此,产后尽早进行母乳喂养对妊娠期母体高血糖的新生儿来说至关重要。新生儿有发生低血糖风险需补充喂养时,使用孕期收集的初乳进行喂养,能够减少配方奶的添加。

孕晚期初乳收集有利于泌乳启动,缩短产后过渡到纯母乳喂养的时间<sup>[23]</sup>。初乳收集由产后提至分娩前,有助于提升产妇母乳喂养信心和自我效能,促进泌乳启动。初乳收集能够软化乳房组织,缓解产后乳房组织充血水肿导致的疼痛,有益于产后母乳喂养时新生儿衔乳,由此提升产后早期纯母乳喂养率<sup>[24-27]</sup>。上述原因可能是孕晚期初乳收集能够提升妊娠期高血糖孕妇在产后24 h及住院期间母乳喂养率的原因。2021年,挪威关于孕晚期初乳收集能够提高妊娠期高血糖产妇住院期间的母乳喂养率的研究与本研究的結果一致<sup>[28]</sup>。

本研究存在一定局限性。本研究中两组新生儿性别有差异,目前尚未发现新生儿性别对妊娠期高血糖孕妇孕晚期初乳收集与产后母乳喂养有影响。试验组孕晚期初乳收集依从性不理想,收集频次未达预期。拟计划通过产后72 h的乳汁乳糖水平判断有无泌乳期延迟,但测量需要至少6 mL母乳,因样本量严重缺失而无法测量。

综上所述,妊娠期高血糖孕妇孕晚期初乳收集

安全可行,实施过程中未发生因初乳收集导致的新生儿不良结局。妊娠期高血糖孕妇孕晚期初乳收集能够降低产后首次喂养配方奶的比例和产后3天的泌乳延迟率,提升产后24 h及产后3天的纯母乳喂养率。本研究的样本量较小,今后需开展大型随机对照试验,以验证妊娠期高血糖孕妇孕晚期初乳收集的安全性及母婴获益。

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