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在线全文

孕早中期体质量指数轨迹与早产之间的因果多中介分析*

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【摘要】 目的 探讨孕早中期体质量指数（body mass index，BMI）轨迹与早产的关联，并探究妊娠期糖尿病（gestational diabetes mellitus，GDM）与炎症因子的中介作用，为早产预防和早期干预提供参考依据。**方法** 采用前瞻性队列研究，选取2018–2021年于重庆市妇幼保健院分娩的孕产妇1 221例。采用组基轨迹模型构建孕早中期BMI轨迹，logistic回归分析及因果中介分析探讨GDM、炎症因子在孕早中期BMI轨迹与早产之间的中介作用。**结果** 共识别出三条BMI轨迹：模式一（48.98%）、模式二（38.41%）和模式三（12.61%）。模式二与模式一轨迹形状相似，但整体水平介于模式一与模式三之间；模式三孕早期处于肥胖水平，随妊娠进展BMI略有下降，孕中期趋稳后小幅回升。在调整协变量后，模式三的早产风险是模式一的3.1倍〔比值比（odds ratio，OR）=3.10，95%置信区间（confidence interval，CI）：1.59～6.06〕。白细胞计数和单核细胞百分比在模式三与早产之间的中介效应具有统计学意义，消除比例分别为0.5%和5.1%。未发现GDM的中介作用。**结论** 孕早中期BMI较高的孕产妇早产的发生风险显著增加，且白细胞计数和单核细胞百分比在其中起中介作用，未发现GDM的中介作用。

【关键词】 体质量变化轨迹 妊娠期糖尿病 炎症 早产

Causal Multiple Mediation Analysis of the Association Between Early and Mid-Pregnancy Body Mass Index Trajectories and Preterm Birth

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[Abstract] Objective To investigate the associations between body mass index (BMI) trajectories in early and mid-pregnancy and preterm birth, to examine the mediating effects of gestational diabetes mellitus (GDM) and inflammatory markers, and to provide evidence for early prevention and intervention of preterm birth. **Methods** A prospective cohort study was conducted and 1 221 pregnant women who delivered babies at Chongqing Maternal and Child Health Hospital between 2018 to 2021 were included. Group-based trajectory modeling was used to identify BMI trajectories in early and mid-pregnancy. Logistic regression and causal mediation analyses were performed to evaluate the mediating effects of GDM and inflammatory factors in the associations between BMI trajectories and preterm birth. **Results** TThree BMI trajectories were identified, and the participants were categorized accordingly into Group 1 (48.98%), Group 2 (38.41%), and Group 3 (12.61%). Group 2 demonstrated a trajectory similar in shape to that of Group 1, with an overall level between those of Group 1 and Group 3. Participants in Group 3 were in the obese range in early pregnancy, with their BMI decreasing slightly along with the progression of pregnancy and stabilizing and then rising slightly in mid-pregnancy. After adjusting for confounders, Group 3 showed higher risks of preterm birth, which were 3.1 times those of Group 1 (odds ratio [OR] = 3.10, 95% CI: 1.59-6.06). Additionally, white blood cell count and monocyte percentage significantly mediated this association, with proportion eliminated of 0.5% and 5.1%, respectively. No mediating effect of GDM was observed. **Conclusion** Pregnant women with higher BMI during early and mid-pregnancy exhibit a significantly increased risk of preterm birth. White blood cell count and monocyte percentage may serve as key inflammatory mediators linking this association while the mediating effect of GDM is not found.

[Key words] Body-mass trajectory Gestational diabetes mellitus Inflammation Premature birth

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早产指妊娠不足37周的活产，它是五岁以下儿童死亡的主要原因之一[1-2]。2020年，全球早产儿约有1 340万，早产率达到9.9%[1]。国内早产率持续上升，最新全国检测数据显示，早产率从2017年的5.1%增至2022年的6.6%[3]。大量研究已证实，早产不仅会增加呼吸窘迫综合征、支气管肺发育不良、坏死性肠炎及癫痫等疾病的风险，还会对远期健康造成不良影响[4]。

母体营养与代谢状态是影响妊娠结局的重要因素。孕前体质量、孕期体质量变化与早产发生密切相关[5]。然而，传统研究多依赖孕期总增重这一静态指标评估孕期体质量变化，难以准确捕捉孕期体质量的动态变化过程，也无法识别关键的干预窗口。孕早中期是母体脂肪组织储存、胎儿器官发育的关键阶段，此时期的体质量指数(body mass index, BMI)变化轨迹能更精准地反映母体营养与代谢状态，进而对妊娠结局产生深远影响[6-7]。此外，妊娠期糖尿病(gestational diabetes mellitus, GDM)及免疫炎症不仅影响孕期增重[8]，还会增加早产的发生风险[9-12]。然而，二者在孕早中期BMI轨迹与早产的关联中是否起中介作用，目前尚属研究空白。

因此，本研究拟采用前瞻性队列设计，构建孕早中期BMI轨迹，探究其与早产之间的关联，同时采用因果中介分析方法，揭示GDM和炎症因子在其中的中介机制，为早产的预防与早期干预提供参考依据。

1 资料与方法

1.1 研究对象

研究对象来源于一项前瞻性队列研究。本研究纳入标准：①2018–2021年，妊娠6～13周在重庆市妇幼保健院进行首次产检的孕妇；②完成妊娠早期、妊娠中期、妊娠晚期和分娩后24 h随访调查；③孕产妇没有严重的精神疾病、认知功能障碍或其他妨碍调查完成的情况。排除标准：①流产、死胎；②双胎或多胎妊娠；③孕前患有糖尿病；④缺失孕24～28周内测量的75 g口服葡萄糖耐量试验(oral glucose tolerance test, OGTT)结果；⑤缺失孕24周后的炎症因子数据；⑥孕早中期BMI测量次数<3次。参与者均已签署知情同意书。共有3 288对母婴满足纳入条件，进一步排除后，最终本研究纳入1 221对母婴。本研究经重庆市妇幼保健院医学伦理委员会审查批准〔(2018)伦审(科)020-02号〕，批件有效期12个月。

1.2 研究指标

早产定义为妊娠<37周的活产。用体质量(kg)除以身高的平方(m^2)计算BMI。依据《妊娠期高血糖诊治指南(2022)》标准，在妊娠24～28周进行75 g OGTT检查，若任一时点血糖值达到以下任一阈值即可诊断为GDM：空腹血糖(fasting plasma glucose, FPG)≥5.1 mmol/L，OGTT 1 h血糖≥10.0 mmol/L，OGTT 2 h血糖≥8.5 mmol/L[13-14]。

使用妊娠>24周首次测量的炎症因子指标，包括白细胞(white blood cell count, WBC)、中性粒细胞计数、中性粒细胞百分比、淋巴细胞计数、淋巴细胞百分比、单核细胞计数、单核细胞百分比和血小板。上述炎症指标均经过log转换和z分数标准化处理，以满足正态分布假设并统一尺度[15]。此外，还纳入系统性免疫炎症指数(systemic immune-inflammation index, SII)、中性粒-淋巴细胞比值(neutrophil-lymphocyte ratio, NLR)、血小板-淋巴细胞比值(platelet-lymphocyte ratio, PLR)三种复合炎症指标，计算公式如下：SII=血小板计数×中性粒细胞计数/淋巴细胞计数；NLR=中性粒细胞计数/淋巴细胞计数；PLR=血小板计数/淋巴细胞计数。基于既往研究[5, 16-17]，本研究考虑了孕产妇年龄、教育程度、孕前自评健康状况、胎儿性别、糖尿病及高血压家族史六个混杂因素，均通过孕产妇病历或问卷收集。

1.3 研究方法

1.3.1 孕早中期BMI轨迹

由于我国GDM在孕24～28周行75g OGTT筛查血糖进行诊断[18]，其发生发展和治疗措施可能改变孕期增重模式，为避免反向因果偏倚，使用孕0～24周BMI数据构建轨迹模型。步骤如下：(1)假设孕早中期BMI轨迹的潜在类别数量介于2至7组之间[19-20]；(2)考虑到BMI的非线性变化趋势，分别构建包含线性项、二次项和立方项的轨迹模型；(3)使用lcmm包进行组基轨迹模型(group-based trajectory modeling, GBTM)分析，并依据以下标准筛选最优模型[19]：①赤池信息量准则(Akaike information criterion, AIC)和贝叶斯信息准则(Bayesian information criterion, BIC)数值较小；②平均后验概率应>0.7；③熵值(entropy)应≥0.8；④各轨迹组样本占比≥5%；⑤优先选择较低阶、结构更简洁的模型。

1.3.2 反事实框架下因果多中介分析

采用logistic回归分析探索孕早中期BMI轨迹与早产之间的关联，报告两个模型：模型1：未调整协变量；模型2：调整母亲年龄、教育程度、孕前自评健康状况、胎儿性别、糖尿病及高血压家族史六个协变量。

在反事实框架下，将总效应(total effect, TE)分解为控制直接效应(controlled direct effect, CDE)和部分消除效应(portion eliminated, PE)，中介模型见图1。CDE为控制中介变量后的直接效应，PE表示通过去除中介路径，从总效应中所去除的那部分效应[21]。当CDE与PE方向一致

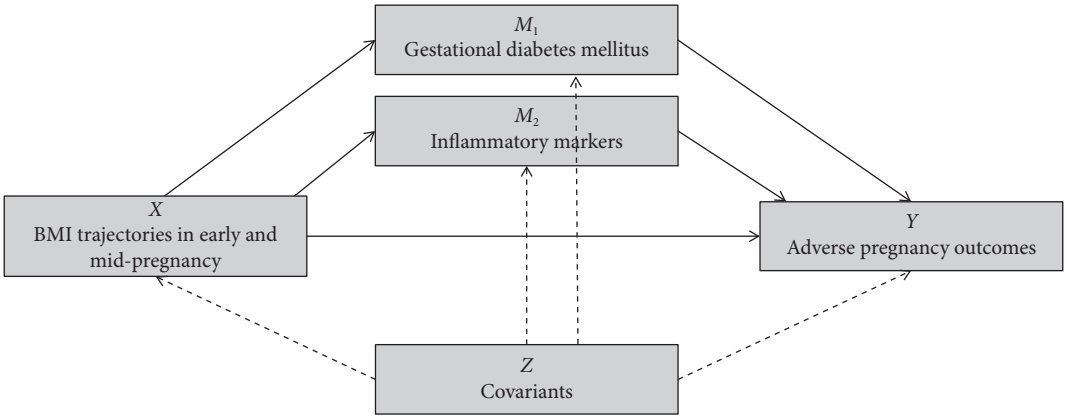

图 1 妊娠期糖尿病、炎症因子及孕早中期BMI轨迹、早产之间的中介模型

Fig 1 The mediating model of the association between gestational diabetes mellitus, inflammatory factors, and BMI trajectories during early and mid-pregnancy with preterm birth

时, 进一步汇报通过中介变量消除的消除比例(proportion eliminated)[22], 计算公式为: 消除比例=(TE—CDE)/(TE—1)。

运用CMAverse包进行因果中介分析, 通过g-formula方法进行参数估计[23]。分别考察各个中介变量在孕早中期BMI轨迹与早产的关联中的中介作用, 每次只纳入一个中介变量进行分析, 模型中额外考虑暴露-中介之间的交互作用, 控制上述六种协变量, 并通过Bootstrap 5 000次自抽样验证来增加模型结果的稳健性。所有统计分析在R软件(version 4.5.1)中完成, $\alpha_{双侧}$=0.05。

2　结果

2.1　孕早中期BMI轨迹

本研究共纳入孕产妇1 221例。基于GBTM所构建的二次项模型在所有候选模型中拟合效果最优, 识别出三条不同的BMI轨迹, 分别是: 模式一(n=598, 48.98%), 模式二(n=469, 38.41%)和模式三(n=154, 12.61%), 见表1、

表 1　确定最佳的孕早中期BMI轨迹模型

Table 1　Identifying the optimal BMI trajectory model for the early and mid-pregnancy

Model	Class	AIC	BIC	Entropy	Group sample/%							Average posterior probability						
					Class 1	Class 2	Class 3	Class 4	Class 5	Class 6	Class 7	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6	Class 7
Linear	1	28 083	28 098	1.00	100.0							1.0						
	2	26 247	26 283	0.83	69.9	30.1						1.0	0.9					
	3	25 578	25 634	0.81	49.9	37.8	12.3					0.9	0.9	0.9				
	4	25 476	25 553	0.72	15.6	43.8	30.4	10.2				0.8	0.8	0.9	0.9			
	5	25 188	25 285	0.77	16.1	30.1	43.1	8.0	2.8			0.8	0.9	0.8	0.9	1.0		
	6	24 993	25 111	0.80	13.7	43.1	9.8	30.1	0.7	2.8		0.8	0.8	0.9	0.9	1.0	1.0	
	7	24 974	25 112	0.76	2.4	29.4	29.5	26.2	9.1	2.8	0.7	0.8	0.8	0.7	0.8	0.9	1.0	1.0
Quadratic	1	28 058	28 078	1.00	100.0							1.0						
	2	26 214	26 260	0.83	69.6	30.4						1.0	0.9					
	3*	25 535	25 607	0.81	49.0	38.4	12.6					0.9	0.9	0.9				
	4	25 269	25 366	0.85	47.6	39.0	10.7	2.8				0.9	0.9	0.9	0.9			
	5	25 133	25 256	0.77	17.1	42.3	29.6	8.4	2.6			0.8	0.8	0.9	0.9	1.0		
	6	24 903	25 051	0.81	13.8	42.3	30.7	9.8	1.0	2.5		0.8	0.8	0.9	0.9	1.0	1.0	
	7	24 883	25 057	0.76	2.2	29.7	28.8	26.4	1.1	9.3	2.5	0.8	0.8	0.7	0.8	1.0	0.9	1.0
Cubic	1	28 061	28 086	1.00	100.0							1.0						
	2	26 269	26 325	0.82	66.8	33.2						1.0	0.9					
	3	26 420	26 507	0.90	0.0	72.7	27.4					NA	1.0	0.9				
	4	26 714	26 831	0.92	0.0	71.7	28.3	0.0				NA	1.0	0.9	NA			
	5	26 675	26 823	0.93	0.0	0.0	73.0	27.0	0.0			NA	NA	1.0	0.9	NA		
	6	26 756	26 935	0.94	0.0	0.0	73.0	27.0	0.0	0.0		NA	NA	1.0	0.9	NA	NA	
	7	26 602	26 811	0.94	0.0	0.0	0.0	73.3	26.7	0.0	0.0	NA	NA	NA	1.0	0.9	NA	NA

AIC: Akaike information criterion; BIC: Bayesian information criterion; NA: not applicable. * The best-performing model.

图2。模式一和模式二轨迹形状相似,但孕早期BMI初始值呈现明显差异,模式一低于20 kg/m^2,模式二孕早期BMI初始值高于20 kg/m^2,因此整体水平高于模式一。模式三在孕早期处于肥胖范围(BMI≥28.0 kg/m^2),但随着妊娠进展BMI呈现轻微下降,至孕中期基本保持稳定,之后略有回升。

GDM、孕产妇文化程度、孕产妇年龄在不同BMI轨迹分组之间差异有统计学(P<0.05),见表2。在总人群中GDM发病率为19.8%,从模式一、模式二到模式三中,GDM的发病率呈逐渐升高的趋势。

2.2 反事实框架下因果多中介分析

在logistic回归分析中,与模式一相比,模式三与早产风险增加显著相关,提示模式三是发生早产的危险因素,见表3。在未调整协变量的模型中,模式三使早产风险增加〔比值比(odds ratio, OR)=2.97, 95%置信区间(confidence interval, CI): 1.55 ~ 5.68, P=0.001〕,调整协变

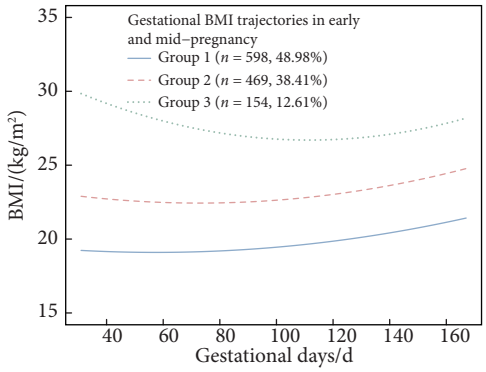

图 2 最佳的孕早中期BMI轨迹(基于GBTM二次项模型)

Fig 2 The optimal BMI trajectory during the early and mid-pregnancy based on the quadratic model of group-based trajectory modeling

表 2 按孕早中期BMI轨迹分组的研究对象基本特征

Table 2 The basic characteristics of the participants grouped by their BMI trajectory during the early and mid-pregnancy

Characteristic	Total	Group 1 (n = 598)	Group 2 (n = 469)	Group 3 (n = 154)	χ^2/Fisher's exact test	P
GDM					36.32	< 0.001
No	979 (80.2)	519 (86.8)	355 (75.7)	105 (68.2)		
Yes	242 (19.8)	79 (13.2)	114 (24.3)	49 (31.8)		
Premature birth					11.82	0.003
No	1 155 (94.6)	574 (96.0)	444 (94.7)	137 (89.0)		
Yes	66 (5.4)	24 (4.0)	25 (5.3)	17 (11.0)		
Maternal education					16.54	0.002
Junior high school or below	44 (3.6)	15 (2.5)	17 (3.6)	12 (7.8)		
Senior high school	117 (9.6)	48 (8.0)	47 (10.0)	22 (14.3)		
College or above	1 060 (86.8)	535 (89.5)	405 (86.4)	120 (77.9)		
Pre-pregnancy self-rated health status					—*	0.285
Very poor	6 (0.5)	3 (0.5)	2 (0.4)	1 (0.6)		
Poor	8 (0.7)	2 (0.3)	4 (0.9)	2 (1.3)		
Fair	243 (19.9)	131 (21.9)	83 (17.7)	29 (18.8)		
Good	713 (58.4)	339 (56.7)	282 (60.1)	92 (59.7)		
Very good	251 (20.6)	123 (20.6)	98 (20.9)	30 (19.5)		
Fetal sex					1.73	0.421
Male	589 (48.2)	277 (46.3)	235 (50.1)	77 (50.0)		
Female	632 (51.8)	321 (53.7)	234 (49.9)	77 (50.0)		
Maternal age					61.45	< 0.001
< 25 yr.	178 (14.6)	114 (19.1)	45 (9.6)	19 (12.3)		
25-30 yr.	632 (51.8)	344 (57.5)	222 (47.3)	66 (42.9)		
> 30 yr.	411 (33.7)	140 (23.4)	202 (43.1)	69 (44.8)		

GDM: gestational diabetes mellitus. The data are presented as case (%). * No statistic calculation needed for Fisher's exact test.

表 3 早产与孕早中期BMI轨迹的关联

Table 3 The association between preterm birth and BMI trajectory during early and mid-pregnancy

BMI trajectories in early and mid-pregnancy#	Model 1		Model 2	
	OR (95% CI)	P	OR (95% CI)	P
Group 2	1.35 (0.76-2.38)	0.309	1.38 (0.76-2.48)	0.289
Group 3	2.97 (1.55-5.68)	0.001	3.10 (1.59-6.06)	0.001

OR: odds ratio. Model 1 is the unadjusted model; Model 2 is adjusted for maternal age, education level, pre-pregnancy self-rated health status, fetal sex, family history of diabetes, and family history of hypertension. # Reference: Group 1.

量后关联增强至3.10倍(OR=3.10, 95%CI: 1.59 ~ 6.06, *P*=0.001)。模式二与早产未表现出显著关联。

因果中介分析结果显示, 白细胞计数和单核细胞百分比在模式三与早产的关联的中介效应具有统计学意义, 见表4。白细胞计数的OR_{TE}为2.97(*P*=0.006), OR_{CDE}为2.96(*P*=0.006), OR_{PE}为0.10(*P*=0.020), 消除比例为0.5%(图3)。单核细胞百分比的OR_{TE}为2.98(*P*=0.006), OR_{CDE}为2.88(*P*=0.008), OR_{PE}为0.15(*P*=0.034), 消除比例为5.1%(图3)。孕早中期BMI轨迹对于中介变量无交互作用。其余中介变量未表现出显著的中介路径。

表 4　妊娠期糖尿病、炎症因子指标在早产与孕早中期BMI轨迹关联中的中介分析结果

Table 4　The mediation analysis results of GDM and inflammatory factors in the association between preterm birth and BMI trajectories during early and mid-pregnancy

Mediator	BMI trajectories in early and mid-pregnancy[#]	OR_{TE}	*P*	OR_{CDE}	*P*	OR_{PE}	*P*
GDM	Group 2	1.75	0.006	1.77	0.010	0.09	0.586
	Group 3	2.96	0.006	3.13	0.018	0.08	0.716
FPG	Group 2	1.76	0.008	1.73	0.010	0.08	0.400
	Group 3	2.97	0.006	3.01	0.009	0.07	0.684
OGTT 1 h plasma glucose	Group 2	1.70	0.012	1.61	0.022	0.16	0.142
	Group 3	2.99	0.003	2.61	0.021	0.26	0.053
OGTT 2 h plasma glucose	Group 2	1.72	0.010	1.65	0.016	0.14	0.082
	Group 3	2.94	0.007	2.73	0.016	0.18	0.053
WBC	Group 2	1.72	0.010	1.72	0.010	0.06	0.235
	Group 3[*]	2.97	0.006	2.96	0.006	0.10	0.020
Platelet count	Group 2	1.74	0.003	1.73	0.003	0.07	0.156
	Group 3	2.95	0.005	2.99	0.006	0.08	0.137
Neutrophil count	Group 2	1.74	0.008	1.74	0.010	0.07	0.128
	Group 3	2.97	0.006	3.01	0.007	0.08	0.144
Neutrophil percentage	Group 2	1.72	0.008	1.72	0.006	0.06	0.338
	Group 3	2.97	0.005	2.97	0.005	0.10	0.067
Lymphocyte count	Group 2	1.72	0.010	1.71	0.011	0.07	0.318
	Group 3	2.96	0.005	2.93	0.006	0.12	0.053
Lymphocyte percentage	Group 2	1.72	0.010	1.73	0.008	0.05	0.410
	Group 3	2.96	0.006	2.99	0.007	0.09	0.070
Monocyte count	Group 2	1.71	0.007	1.74	0.006	0.04	0.505
	Group 3	3.03	0.004	3.01	0.006	0.11	0.072
Monocyte percentage	Group 2	1.69	0.011	1.70	0.007	0.05	0.509
	Group 3[*]	2.98	0.006	2.88	0.008	0.15	0.034
SII	Group 2	1.74	0.006	1.74	0.006	0.06	0.247
	Group 3	2.96	0.005	3.04	0.007	0.06	0.194
NLR	Group 2	1.72	0.006	1.74	0.006	0.05	0.488
	Group 3	2.99	0.005	3.01	0.006	0.10	0.060
PLR	Group 2	1.72	0.010	1.72	0.008	0.07	0.301
	Group 3	2.96	0.007	2.96	0.010	0.10	0.051

GDM: gestational diabetes mellitus; FPG: fasting plasma glucose; OGTT: oral glucose tolerance test; WBC: white blood cell count; SII: systemic immune-inflammation index; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; OR: odds ratio. [*] *P* values of total effect (TE), controlled direct effect (CDE) and portion eliminated (PE) were all < 0.05, indicating significant mediation pathways. [#] Reference: Group 1.

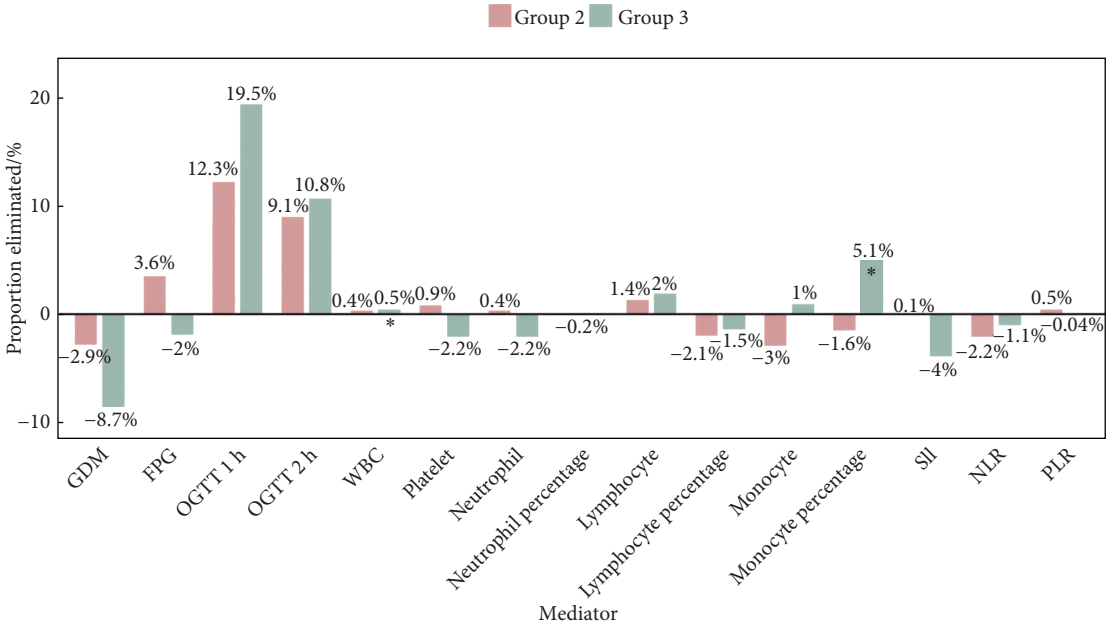

图 3 孕早中期BMI轨迹对早产影响的消除比例

Fig 3 The proportion eliminated of the effect of BMI trajectories during early and mid-pregnancy on preterm birth

The abbreviations are explained in the note to Table 2. * Indicates a significant mediation path.

3 讨论

本研究最终识别出三种孕早中期BMI轨迹，处于较高BMI轨迹组(模式三)发生早产的风险是较低BMI轨迹组(模式一)的3.10倍。白细胞计数、单核细胞百分比在模式三与早产之间起中介作用，消除比例分别为0.5%、5.1%。此外，孕早中期BMI轨迹对于中介变量无交互作用。

既往少有研究探究孕早中期BMI轨迹与早产的关联，且现有研究结果尚存争议。广州的一项研究发现，孕早期增重过多可能会增加早产的发生风险，是孕早期增重适宜组的2倍(OR=2.00, 95%CI: 1.32 ~ 3.00)[24]，与本研究结果基本一致。相反，有研究发现孕早中期增重较低的轨迹组发生早产的风险更高(OR=1.28, 95%CI: 1.05 ~ 1.63)[25]。也有研究报告孕期增重与早产之间呈“U”型关联，即孕期增重过少或过多均能增加发生早产的风险[26-27]。另有研究未发现孕期体质量轨迹与早产之间存在显著关联[28-29]。

传统的中介分析多是基于系数乘积法估计间接效应，如广义结构方程模型，但其应用存在诸多限制条件。与传统的中介分析相比，基于反事实框架的因果中介分析的优势不仅在于它适用于任何类型的中介变量和结局变量，还能评估传统方法难以处理的暴露-中介变量的交互作用，因此具有更广泛的实用性和灵活性。本研究基于反事实框架下的因果中介分析方法进一步发现，白细胞计数和单核细胞百分比可能构成孕早中期BMI轨迹影响早产的重要炎症通路。既往研究发现，妊娠期炎症相关信号传导通路的异常激活及炎症因子生成与早产发生密切相关[30]。白细胞计数作为体内炎症反应的标志物，其异常升高提示机体处于炎症状态[9]。这一发现与LIU等[31]研究一致，提示炎症可能是连接母体肥胖与早产的重要机制。单核细胞则参与胎盘发育，在分娩中也发挥作用，其占比异常升高可能提示妊娠过程出现异常[32]。孕早中期较高的BMI轨迹可能导致机体因脂肪细胞肥大而处于慢性炎症状态，再通过单核细胞活化，促进子宫收缩、宫颈成熟、胎膜破裂等生理变化，最终诱发早产[30]。

本研究还发现，孕早中期体质量更高、增重速率过快均会增加GDM的发生风险，这与既往研究一致[8, 24]。然而，本研究并未发现GDM及相关血糖指标介导孕早中期BMI轨迹与早产的关联，但GDM的存在可能通过影响孕晚期增重模式，或与炎症因子协同作用[33]，形成“代谢-免疫”双通路机制，从而诱发早产。此前也有研究发现GDM部分介导了孕前肥胖与自然早产之间的关联[31, 34]。PREDA等[12]系统综述也强调了GDM与早产关系中炎症通路的关键作用。这一复杂过程仍需进一步研究。

本研究的优势在于采用前瞻性队列设计，减少回忆偏倚；通过构建BMI动态轨迹更真实反映了孕早中期体质量变化对早产的影响；运用因果中介分析方法揭示GDM、炎症因子的中介机制。本研究亦存在局限：因数据库的限制，未探讨C反应蛋白、细胞因子等炎症标志物的中介作用；尽管控制了六种协变量，但未被控制的混杂因素仍可能存在；其三，无法探究GDM与炎症因子之间

是否存在交互作用。未来研究可扩大样本、增加更多的炎症指标、结合代谢组学数据，以进一步验证“孕早中期BMI轨迹-代谢/炎症-早产”的因果中介机制。

综上所述，孕早中期BMI较高的孕产妇早产的发生风险显著升高，且该关联部分通过白细胞计数和单核细胞百分比介导。强化孕期体质量管理与代谢炎症监测，对于降低早产风险具有重要的公共卫生意义。

*　　*　　*

作者贡献声明　杨天负责论文构思、数据审编、正式分析、研究方法、可视化和初稿写作，曹彧恒负责数据审编、研究方法、验证和审读与编辑写作，周文正负责调查研究和提供资源，肖成汉负责研究方法、监督指导和验证，刘振谧负责经费获取、调查研究、研究项目管理、监督指导和审读与编辑写作。所有作者已经同意将文章提交给本刊，且对将要发表的版本进行最终定稿，并同意对工作的所有方面负责。

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