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妊娠期肥胖对妊娠结局及新生儿影响的研究进展

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摘　要

全球范围内，妊娠期肥胖的发生率持续上升，妊娠期肥胖不仅增加妊娠期糖尿病、妊娠期高血压疾病、巨大儿及剖宫产率等孕产妇和胎儿近期不良结局的发生风险，还可能通过宫内编程机制对母体及其子代的远期代谢健康产生深远影响。本文系统综述了妊娠期肥胖对妊娠结局及新生儿健康的影响，旨在为临床管理和干预策略的制定提供参考依据。

关键词

妊娠期肥胖，妇幼健康，妊娠结局

Advances in Understanding the Impact of Gestational Obesity on Pregnancy Outcomes and Neonatal Health

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Abstract

The prevalence of gestational obesity has been rising globally. Gestational obesity not only increases the risk of short-term adverse outcomes for pregnant women and fetuses—including gestational diabetes mellitus, hypertensive disorders of pregnancy, macrosomia, and increased cesarean section rates—but may also profoundly affect the long-term metabolic health of both mother and offspring through

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intrauterine programming mechanisms. This review systematically examines the effects of gestational obesity on pregnancy outcomes and neonatal health, with the aim of informing clinical management and intervention strategies.

Keywords

Gestational Obesity, Maternal and Child Health, Pregnancy Outcomes

1. 引言

妊娠期肥胖已成为一个重大的公共卫生问题，对妊娠、分娩以及母婴双方的长期健康产生显著影响，以及对母体和子代的长期健康产生影响[1]。根据最新全球系统综述与 Meta 分析数据，2010~2019 年间全球妊娠期肥胖患病率已达 16.3% (95%CI: 15.1%~17.5%)，合并超重与肥胖的患病率更高达 43.8% (95%CI: 42.2%~45.4%)，线性回归模型预测，至 2030 年全球妊娠期肥胖患病率将攀升至 23.3% [2]。

妊娠期肥胖不仅直接增加母体妊娠期糖尿病、子痫前期、难产及产后出血等并发症风险[3]，更通过宫内编程机制，对子代产生跨代际的深远影响，Barker 假说指出，生命早期 1000 天(从受孕至出生后 2 岁)的营养环境可通过表观遗传修饰、代谢适应及器官结构重塑等途径，永久改变个体的基因表达模式与代谢表型，使胎儿在宫内即“预测”并适应预期的产后环境，当这种预测与出生后实际的能量环境不匹配时，便显著增加代谢综合征、2 型糖尿病及心血管疾病等慢性非传染性疾病的易感性[4]。

鉴于妊娠期肥胖已成为一个具有跨代际影响的公共健康问题，深入解析其对母体及子代远期健康的双重影响机制，对于制定基于生命历程理论的早期干预策略、阻断肥胖的代际循环具有重要科学价值与临床意义。本文系统综述妊娠期肥胖对母子远期代谢、心血管及肿瘤风险的影响，重点阐述其子代从宫内编程到成年期代谢表型的分子机制，并探讨当前干预策略的证据。

2. 对妊娠期并发症的影响

脂肪组织是活跃的内分泌器官。妊娠期脂肪过多时，可导致很多器官系统发生代谢通路、血管通路以及炎症通路的失调，从而影响产科结局[5] [6]。例如，肥胖相关胰岛素抵抗和炎症通路异常可影响胎盘发育和功能，还与子痫前期的发生有关[7]-[9]。研究发现，母亲越肥胖，一些肥胖相关妊娠并发症的风险就越大[10]。

2.1. 妊娠期糖尿病(Gestational Diabetes Mellitus, GDM)

在众多妊娠并发症中，妊娠期糖尿病(GDM)与肥胖的关系最为密切。研究表明，肥胖女性的 GDM 风险显著高于正常体重的产科人群[11]，且这一风险随孕前体重和 BMI 的增加而升高。一篇系统评价显示，BMI 每增加 1 kg/m^2，GDM 的发生风险增加 0.92% [12]。这种风险的升高主要归因于肥胖状态下生理代谢的改变。肥胖女性在妊娠前或妊娠早期存在一定程度的胰岛素抵抗，而妊娠本身作为一种“生理性应激状态”，进一步加重胰岛素抵抗程度，从而诱发或加剧糖代谢异常[13]。此外，并非所有肥胖个体的代谢表型相同。相较于代谢健康的肥胖孕妇，那些处于代谢不健康状态(如伴有高血脂、高血压或慢性炎症)的肥胖女性，发生 GDM 的风险更高[14]。这提示我们，在妊娠期保健中，除了关注体重绝对值，也应重

视肥胖人群的代谢特征评估，以便更精准地识别高危人群并实施早期干预。

2.2. 妊娠期高血压疾病

肥胖与子痫前期的关联已成为产科领域的重要研究方向。研究一致表明，母亲孕前 BMI 是子痫前期及妊娠期高血压疾病的独立危险因素[15]。一项纳入 13 项队列研究、涵盖近 140 万名孕妇的系统综述进一步证实，妊娠前 BMI 每增加 5~7 kg/m^2，子痫前期的发生风险即增加约一倍[16]。

尽管肥胖与子痫前期的关联已得到流行病学研究的广泛证实，其背后的病理生理机制尚未完全阐明。现有研究提示，这种关联可能源于肥胖状态下多种代谢异常的共同作用。肥胖可诱发胰岛素抵抗、血脂异常、全身性炎症反应增强及氧化应激等病理生理改变，这些改变不仅增加母体的心血管负担，还可能通过影响胎盘的发育与功能，进而促进子痫前期的发生[17]。特别是，脂肪组织能产生丰富的促炎症细胞因子，促进母体抗血管生成因子的表达，破坏血管生成的动态平衡，这或许是连接肥胖与子痫前期的重要分子机制之一。

2.3. 剖宫产率

肥胖是导致计划性剖宫产及产时剖宫产的重要危险因素，且这一风险随着母体 BMI 的升高而显著增加[18]。这一关联已得到多项流行病学研究的证实。一篇涵盖 12 个国家、纳入 97,518 名孕妇的系统综述与 Meta 分析显示，与正常体重孕妇相比，超重和肥胖孕妇的剖宫产风险分别增加 35% (aOR 1.35, 95% CI 1.24~1.49)和 77% (aOR 1.77, 95% CI 1.49~2.11)，且随着肥胖等级加重，风险呈剂量效应关系，I 级、II 级和 III 级肥胖孕妇的剖宫产风险分别增加 78%、121%和 161%，超重孕妇的急诊剖宫产风险亦显著升高(aOR 1.34, 95% CI 1.02~1.76) [19]。

肥胖增加剖宫产风险的机制是多方面的。首先，肥胖孕妇更易合并各类妊娠并发症，如妊娠期糖尿病和妊娠期高血压疾病，这些并发症本身即增加了剖宫产的医学指征[20]。其次，肥胖常伴随胎儿生长加速，巨大儿的发生率显著升高，与正常体重组相比，超重女性巨大儿风险显著增加(OR = 1.66, 95% CI 1.35~2.01)，肥胖女性同样风险显著增加(OR = 1.66, 95% CI 1.13~2.45)，而低体重女性风险显著降低(OR = 0.55, 95% CI 0.41~0.73) [21]，这可能导致头盆不称。第三，肥胖可影响产程的正常进展，研究显示，肥胖孕妇腹肌收缩力减弱，易发生低张性宫缩乏力，导致产程延长或滞产，同时，肥胖相关炎症状态可能影响子宫平滑肌的收缩功能，降低子宫对催产素的敏感性[22]。综上上述因素共同作用，肥胖孕妇的剖宫产风险显著高于正常体重孕妇[20] [23]。

从临床实践角度而言，有研究估算，在超重和肥胖孕妇中，分别有 25.9%和 43.5%的剖宫产分娩分别归因于产妇超重和肥胖[19]。这一数据提示，孕前及孕期体重管理对于降低剖宫产率、改善分娩结局具有重要意义。

3. 对胎儿及新生儿的影响

母亲肥胖可能影响后代的远期结局，胎儿在发育过程中暴露于高水平的葡萄糖、胰岛素、脂质和炎症细胞因子会诱导表观遗传学改变。这些宫内效应可能导致代谢程序化(metabolic programming)发生永久或短暂性变化，导致后代成年后出现不良健康结局，即胎儿源性成人疾病理论(Barker 假说) [24] [25]。然而，由于母体代谢环境与发育中胎儿的复杂关系，以及产后因素的影响(包括生活方式和环境)，很难对肥胖潜在的程序化作用进行研究[26]。

3.1. 先天性畸形

肥胖孕妇所孕育的胎儿发生先天性结构异常的风险显著增加，常见的畸形包括神经管缺陷(neural

tube defects, NTDs)、先天性心脏畸形、口面部裂(如唇裂和腭裂)以及肢体短缩畸形[27]。这种风险随着孕妇肥胖程度的加重而升高。一篇系统综述与 Meta 分析显示，与正常体重孕妇相比，肥胖孕妇胎儿发生神经管缺陷的风险增加 87% (OR = 1.87, 95% CI: 1.62~2.15)，其中脊柱裂的风险增加 124% (OR = 2.24, 95% CI: 1.86~2.69)，心血管畸形的风险增加 30% (OR = 1.30, 95% CI: 1.12~1.51)，唇腭裂风险增加 20% (OR = 1.20, 95% CI: 1.03~1.40)，肢体短缩畸形风险增加 34% (OR = 1.34, 95% CI: 1.03~1.73) [27] [28]。

3.2. 围产期死亡率

肥胖对围产儿的影响涉及从胎儿期至婴儿期的全程健康风险，即使是 BMI 的适度增加，也会显著增加胎儿、新生儿死亡风险。一项 Meta 分析显示，与 BMI = 20 kg/m^2 的正常体重孕妇相比，BMI = 25 kg/m^2 (超重)和 BMI = 30 kg/m^2 (肥胖)孕妇的胎儿死亡绝对风险分别增至每 10,000 例妊娠 82 例和 102 例(正常体重组参考值为 76 例)；死产绝对风险则分别达 48 例和 59 例(正常体重组参考值为 40 例) [29]。

肥胖增加围产儿死亡风险的核心机制可能是睡眠呼吸障碍介导的慢性缺氧损伤。肥胖孕妇阻塞性睡眠呼吸暂停(obstructive sleep apnea, OSA)的发病率显著高于正常体重人群，其核心病理特征为夜间反复出现的呼吸暂停(持续 ≥10 秒)及间歇性低氧血症(血氧饱和度下降 ≥3%)。这种慢性间歇性缺氧状态可直接干扰子宫－胎盘循环的氧供稳定性，导致胎盘氧输送不足，进而诱发胎儿宫内缺氧、代谢紊乱，最终显著增加死产及新生儿死亡风险。

3.3. 巨大儿及大于胎龄儿

妊娠期肥胖作为重要的孕前代谢危险因素，与胎儿过度生长密切相关，可显著增加巨大儿(出生体重 > 4000 g)及大于胎龄儿(large for gestational age, LGA)的发生风险，且该效应独立于妊娠期并发症存在[30]。一项 Meta 数据分析显示：孕前体重与新生儿出生体重呈线性正相关，孕前肥胖孕妇分娩 LGA 的风险显著高于正常体重孕妇[31]。即便剔除妊娠期糖尿病(gestational diabetes mellitus, GDM)已知可干扰胎儿生长的妊娠期并发症后，孕前肥胖与胎儿生长指标异常、巨大儿及 LGA 的关联性仍持续存在[32]。这些发现提示孕前肥胖可独立介导胎儿宫内过度生长，是导致不良出生体重结局的关键危险因素。

3.4. 儿童期肥胖和心血管代谢疾病

在肥胖环境中发育可能导致胎儿代谢途径的永久性改变，从而增加儿童和成年期疾病的风险，如高血压、高血糖和胰岛素抵抗、高脂血症、肥胖和冠状动脉疾病、肥胖、脂肪组织过多，以及代谢相关脂肪性肝病(metabolic dysfunction-associated steatotic liver disease, MASLD) [33]。不过，一些相同的遗传因素或家庭生活方式也在这些疾病的发生中起到一定作用。

3.5. 神经发育

最近的证据表明，产前和哺乳期暴露于母体肥胖与后代的精神疾病和神经发育障碍有关，即焦虑和抑郁、精神分裂症、注意力缺陷多动障碍、自闭症谱系障碍和认知障碍[33]-[36]。这种关联的可能机制包括胰岛素、葡萄糖、瘦素、多巴胺和 5-羟色胺信号传导的失调，神经炎症和增加的氧化应激。

研究发现，超重/肥胖孕妇的子女发生脑瘫的风险升高。一篇 Meta 分析纳入 8 项队列研究和病例对照研究，包括近 800 万例参与者，报道超重、肥胖和 III 度肥胖母亲的后代发生脑瘫的相对危险度分别是 1.29、1.45 和 2.25 [37]。其中一项人群队列研究显示，该风险的增加似乎在一定程度上与窒息相关新生儿并发症有关[38]，而这些并发症在超重和肥胖母亲所生孩子中更常见[39]。同一研究组报道，超重和肥胖女性的后代易患上儿童期癫痫，校正了多个母亲和新生儿混杂因素后，这种倾向有所减弱但依然存在[40]。

4. 妊娠期肥胖对母亲远期健康的影响

4.1. 代谢系统：从妊娠期糖尿病到终身代谢紊乱

妊娠期肥胖是母体远期代谢功能障碍的最强预测因素之一。最新系统综述证实，妊娠期肥胖女性远期发生 2 型糖尿病(T2DM)的风险显著升高[41]，且与肥胖程度呈剂量–反应关系。一项涵盖韩国全国队列的大型研究显示，妊娠期肥胖与妊娠期糖尿病(GDM)存在显著交互作用，肥胖组中妊娠期糖尿病患者的 2 型糖尿病风险(风险比 2.84)高于非肥胖组(风险比 2.31)，与既无肥胖也无妊娠期糖尿病者相比，同时患有肥胖和妊娠期糖尿病者发生产后 2 型糖尿病的风险增加 7.59 倍[42]。这表明肥胖与 GDM 对母体远期糖代谢损害具有协同放大效应。

产后代谢综合征(MetS)的进展轨迹更为隐匿但危害深远。妊娠期肥胖诱导的代谢损伤具有“记忆效应”，即使体重部分恢复，胰岛素抵抗和脂代谢紊乱仍持续进展[7]。

产后体重滞留是连接妊娠期肥胖与远期代谢风险的关键环节。研究显示，GDM 女性产后早期(6~8 周)平均体重滞留 4.8 ± 6.0 kg，至产后 1 年仍维持 4.2 kg (95% CI: 0.7~8.4)的显著正平衡。这种体重轨迹不仅增加再次妊娠的并发症风险，更通过脂肪组织的慢性炎症状态，形成“肥胖–妊娠–更严重肥胖”的恶性循环[43]。

4.2. 心血管系统

妊娠期肥胖对心血管系统的损害具有“双重打击”。妊娠期已存在的血流动力学负荷叠加肥胖相关的低度炎症，导致血管内皮功能急性损伤并持续至产后。研究表明，产后 5 年内 GDM 组心血管疾病累积发病率高于单纯肥胖组，但 5 年后出现逆转，单纯肥胖组反超。这提示妊娠期肥胖的心血管损害具有延迟显现效应，远期风险甚至超过 GDM 本身[42]。

妊娠期高血压疾病与肥胖的协同作用进一步放大心血管风险。一项在肯尼亚开展的产后 6 个月前瞻性队列研究发现，合并妊娠期高血压或子痫前期的女性，产后 MetS 风险为血压正常者的 3.01 倍(95% CI: 1.58~5.71)，具体表现为高血压风险增加 3.35 倍、高甘油三酯血症增加 3.25 倍、空腹高血糖增加 6.20 倍[44]。考虑到肥胖是妊娠期高血压的主要危险因素，这种叠加效应在肥胖人群中尤为突出。

5. 病理生理机制

妊娠期肥胖不仅是代谢紊乱的表现，更通过多种分子通路对母体与胎儿产生深远的程序化影响。近年研究从表观遗传修饰、线粒体功能障碍及肠道菌群失调三个维度揭示了其核心机制。

5.1. 表观遗传修饰

表观遗传机制是连接母体代谢环境与胎儿基因表达调控的关键纽带。妊娠期肥胖相关的慢性炎症和高血糖状态可诱导 DNA 甲基化模式改变、组蛋白修饰及非编码 RNA 表达异常[45]。这类表观遗传改变可持续至子代出生后，增加儿童期肥胖、心血管疾病及神经发育障碍的风险[46]。

5.2. 线粒体功能障碍

线粒体作为细胞能量代谢的核心，在妊娠期肥胖状态下呈现结构损伤与功能减退[47]。母体高脂暴露可导致胎儿肝脏线粒体氧化磷酸化能力下降，脂肪酸 β-氧化受损，进而促进脂质异位沉积[48]。线粒体动态失衡(分裂与融合异常)伴随活性氧过量产生，进一步激活炎症信号通路[49]。此外，线粒体 DNA 拷贝数减少和氧化磷酸化复合物活性降低也被证实参与胎盘功能不全的发生[48]。

5.3. 肠道菌群失调

肠道菌群在妊娠期肥胖的发病机制中扮演核心角色。肥胖孕妇肠道菌群多样性显著降低，条件致病菌属升高，而部分有益菌减少[50]。L-茶氨酸干预实验发现，妊娠期肥胖小鼠的肠道屏障功能受损，L-茶氨酸给药可改善代谢紊乱和不良妊娠结局[51]，确立了菌群失调与妊娠结局之间的因果联系。

上述三种机制并非独立发挥作用。肠道菌群代谢产物可影响表观遗传修饰酶的活性，线粒体功能改变又能反作用于菌群组成。

6. 干预策略与未来展望

针对妊娠期肥胖的干预需覆盖孕前、孕期和产后三个时间点，目前研究集中在生活方式干预和药物辅助治疗两大方向。

6.1. 生活方式干预

孕前是优化体重的理想窗口，但相关研究较为有限。现有证据表明，孕前减重 10%可显著降低妊娠期糖尿病和子痫前期风险[52]。然而，对于计划妊娠的肥胖女性，强化生活方式干预的长期依从性面临挑战。

孕期生活方式干预包括饮食调整及运动，这有助于控制孕期增重过多。在孕期进行每周 3~7 次、每次约 30~60 分钟有氧运动，可显著降低早产及妊娠期糖尿病发生[53]。但过于严格的限食可能增加小于胎龄儿风险，提示干预需以适宜增重为目标而非减重。

产后是阻断肥胖代际传递的关键期。帮助产妇努力减去妊娠期和妊娠前增加的体重、避免产后增重，达到健康 BMI。达到健康 BMI 能改善整体健康，还能降低再次妊娠时出现肥胖相关妊娠并发症的风险[53]。

6.2. 二甲双胍的应用

二甲双胍作为胰岛素增敏剂，在妊娠期肥胖管理中的应用受到广泛关注。针对无糖尿病的肥胖孕妇，研究显示二甲双胍可显著降低孕期增重但未改变新生儿出生体重[54]。

二甲双胍能够自由透过胎盘，胎儿血药浓度可达母体水平，虽然尚未发现二甲双胍会增加先天畸形风险，但胎儿体内二甲双胍浓度与母体相等，且二甲双胍可抑制生长、抑制线粒体呼吸、对基因表达产生表观遗传修饰、模拟胎儿营养限制，并改变出生后糖异生反应[55]。用药前应告知患者尚不明确药物穿过胎盘的远期影响，包括对胎儿编程的可能影响。

6.3. 未来展望：精准分型与多靶点整合

未来的研究需着力于以下几个方向：基于代谢表型(如胰岛素抵抗程度、菌群类型、炎症标志物)对肥胖孕妇进行分层，识别最可能从二甲双胍等药物干预中获益的亚群。开展长期、标准化的子代随访，明确宫内药物暴露对青春期及成年期代谢健康的真实影响。开发孕期安全的代谢调节剂，L-茶氨酸在动物实验中显示出调控菌群–胆汁酸通路的潜力，但其临床转化仍需验证。整合生活方式、药物与新兴生物制剂的序贯或联合策略，有望打破肥胖的代际传递链条。总而言之，妊娠期肥胖对母儿的影响贯穿整个围产期，并可能延伸至子代的远期健康。无论是从降低即刻的产科风险，还是从阻断不良健康状态的代际传递角度出发，孕前体重管理都应是妇幼保健工作的重中之重。即使是在孕前或孕早期进行适度的体重控制，也能带来显著的临床获益。针对肥胖孕妇制定详细的孕期筛查、监测与干预流程，以改善这一高风险群体的整体妊娠结局。

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