

早产因素的国内外研究进展

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摘 要

早产的全球发生率约为12%，是新生儿死亡的主要原因。被证实的导致早产的原因很多，如子宫胎盘缺血或出血、既往早产史、宫颈长度较短以及炎症和感染等。早产是一个复杂的全球性公共卫生问题，其发生率和影响因素多样，预测和预防早产仍是产科研究的重要课题，本文总结了近些年来导致早产的因素，以供广大产科同仁参考。

关键词

早产, 孕妇, 新生儿

Research Progress on the Factors of Preterm Birth at Home and Abroad

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Abstract

The global incidence of premature birth is about 12%, which is the leading cause of neonatal mortality. There are many proven causes of premature birth, such as uterine and placental ischemia or bleeding, a history of premature birth, short cervical length, and inflammation and infection. Premature birth is a complex global public health issue with diverse incidence and influencing factors. Predicting and preventing premature birth remains an important topic in obstetric research. This article summarizes the factors that have led to premature birth in recent years for reference by obstetric colleagues.

Keywords

Premature Birth, Pregnant Women, Newborns

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1. 引言

WHO 定义早产是指发生在胎龄不到 37 周的分娩。早产的死亡率为 75% [1], 即使存活下来他们相较于足月产出现神经发育障碍以及呼吸系统和消化系统并发症的风险也会增加, 选择准确的、有针对性的干预措施能够减少早产的发生[2] [3]。最新调查显示在全球多地早产的发生率高于 10% [2] [4] [5]。随着社会的不断发展, 医疗技术及经济水平的提高, 目前胎儿存活阈值降低, 从而导致总体早产率明显增加[6]。中国的早产率约为 10%, 2012 年复旦大学中国新生儿协作网的新生儿出生数据显示, 在中国, 早产儿发生率居高不下, 华中、华南及西南等地区高达 12.46% [7]。美国的早产率为 12%~13%, 研究认为黑人、非裔美国人和非裔加勒比人的早产风险是其他种族或民族妇女的三到四倍, 导致美国的综合早产率升高[8]; 但欧洲和其他发达国家的早产率为 5%~9%, 究其原因可能为优质的产前护理[9]。研究发现多种原因可引起早产, 包括子宫胎盘缺血或出血、子宫过度扩张、应激、既往早产史、黑人种族、母亲低体重指数、宫颈长度较短、宫颈 - 阴道胎儿纤连蛋白浓度升高以及炎症和感染等[10]。多项研究显示妊娠合并无症状菌尿会增加早产的风险[11], 但也有研究认为无症状菌尿与早产的发生无关[12]。

2. 早产的因素

2.1. 高龄

高龄产妇是指母亲分娩时年龄大于 35 岁。无论是在低收入或高收入国家, 高龄均被认为是导致早产的主要风险因素[13] [14]。研究显示, 年龄大于 35 岁早产发生率明显增加[2], Jacobsson 等人认为 40 岁以上产妇围产儿死亡率、胎儿宫内死亡率、新生儿死亡率均高于孕龄产妇, 此外随着产妇年龄的增加, 早产率及先兆子痫发生率也会增加[15]。同时随着年龄增加, 产妇的妊娠并发症及合并症如妊娠期高血压疾病、妊娠期糖尿病、前置胎盘等的发生率均升高[16] [17], 对于高龄妊娠, 应做好健全的妊娠前评估及准备。

2.2. 体重指数

体重指数的极端范围(BMI, 以公斤为单位的体重除以以米为单位的身高的平方)(BMI 低于 18.5 或大于 30)被认为是自发性早产的危险因素。低体重指数可能与慢性营养不良有关, 缺乏铁或锌营养元素, 可能会对胎儿出生体重和免疫系统的发育造成负面影响, 从而导致早产[3] [14]。体重指数超过 30 后, 每增加 5, 早产风险成倍增加[18]。Khatibi 等人认为不管肥胖或超重孕妇的体力情况如何, 均不会降低早产风险[19]。对于 BMI 超重的备孕期女性, 孕前的体重控制、健康习惯及必要的体力活动能够减少孕期多项疾病的风险。

2.3. 吸烟

吸烟会增加多项疾病的患病风险, 妊娠早期吸烟的妇女不仅会增加早产风险, 而且发生妊娠 28 周前

极早产的风险增加 20% [3]。吸烟导致早产的风险会随着戒烟的早晚与吸烟量的减少而减少[14]，美国最近一项回顾性研究表明，如果女性在怀孕早期戒烟，无论是在怀孕的前三个月还是中期，早产的风险都不会增加。然而，将戒烟推迟到怀孕后期，或者在整个怀孕期间继续吸烟，都会显著增加早产的风险。所以，在怀孕早期戒烟可以消除这种风险，在全国范围内推广孕早期戒烟计划可能会对降低早产率产生重大影响[20]。多项研究表明，单独的尼古丁戒断，比如电子烟，并不会降低早产的发生率[21] [22]。目前我国育龄期女性吸烟率逐渐增加，全国推广育龄期女性限制吸烟政策能够降低妊娠妇女围生期及新生儿各类疾病的发生。

2.4. 精神、心理因素

多项研究表明，抑郁、焦虑和母亲的压力与早产风险的增加显著相关[14] [23]。妊娠期间，雌孕激素水平的变化会导致孕妇情绪波动性增大，家庭、工作单位及社会对于孕妇的关怀及福利政策有助于缓解、降低孕妇的情绪波动及抑郁焦虑心情。

2.5. 既往早产史

Ferrero 等人的研究显示有过早产史的女性相比于无早产史的女性再次怀孕时再次早产的风险大约高出 4~6 倍，前次早产孕周越小，再次早产风险越高[3]。多次早产发生的风险与胎儿的数量有关，单胎早产后怀孕单胎早产的风险低于多胎早产后怀孕单胎的一倍，而多胎早产后怀孕单胎的风险最高。同时每一次早产均会增加下次怀孕早产的风险[24] [25]。

2.6. 刮宫术

刮宫终止妊娠是早产发生的独立危险因素，是刮宫后继发的宫颈创伤造成的，在非手术流产后可能会减少[26]。

2.7. 宫颈因素

宫颈锥切术或宫颈切除术等宫颈手术，可增加早产的风险，其原因可能与手术操作或感染导致发育不良有关。在妊娠中期测量宫颈长度可以预测再次妊娠早产的风险[27] [28]。目前已经证实宫颈长度越短，早产发生率越高[29]；Fonseca 等人的研究显示宫颈长度 < 15 mm，早产发生率增加到 34% [14]。虽然像黄体酮等治疗已经证实能够降低早产的风险，但由于低风险孕妇发生宫颈管缩短的风险较低，同时能够预测早产发生的准确率较低，孕期常规筛查宫颈管长度仍存在争议[30]-[33]。但对于既往早产的孕妇，宫颈管缩短的发生率较高，筛查宫颈管长度预测早产的敏感性为 70%，同时能够指导激素治疗，所以对于上述人群进行宫颈筛查是必要且有意义的[34]-[38]。

2.8. 子宫畸形

子宫畸形妇女早产的风险总体上约为 40%。畸形严重程度的不同早产发生风险也不同，子宫发育迟缓妇女的早产风险为 56%，单角子宫妇女的早产风险为 43%，双角子宫妇女的早产风险为 39%，子宫纵膈妇女的早产风险为 31% [39]。纵膈子宫行纵膈切除可降低早产风险，使足月分娩率增加到 75%，活产率 85%，故而对于孕前筛查出妇科疾病的备孕女性，积极治疗可以降低围产期相关疾病发生的风险[40]。

2.9. 胎儿畸形

胎儿畸形与早产风险增加有关，Brown 等人研究发现一些特殊的胎儿畸形，比如消化系统畸形导致的羊水过多会增加早产的风险，有缺陷婴儿的早产风险为 21.5%，而没有缺陷的婴儿早产风险为 9.3% [41]。

多数胎儿重大畸形在系统超声筛查发现时进行了引产，从而减少了家庭及社会的负担。

2.10. 多胎妊娠

研究发现，多胎妊娠使早产的风险明显增加。大多数双胎分娩发生在中期早产期(妊娠 32~33 周)和晚期早产期(34~36 周)内。在所有双胎妊娠中，中期早产率为 14.5%，晚期早产率为 49.8%，足月出生率为 35.7% [42]。在美国，双绒毛膜双胎 32 周前早产率为 5%，单绒毛膜双胎为 10%。近年来，双胎的早产率近 50%，三胎的早产率高达 90%。故如若减少胚胎移植的数量，对有效降低早产的发生率是至关重要的 [3]。作者认为政府及地区级孕保单位应加强对多胎妊娠女性的围产期筛查及预防工作，从而减少多胎妊娠和早产的发生率。

2.11. 宫内感染

羊膜腔内感染是指羊水中检测到微生物存在的炎症反应，是自发性早产的主要原因之一，在胎膜完整早产的孕妇中发生率约为 30%，在胎膜早破早产孕妇中发生率高达 60% [43]-[47]。研究发现，妊娠期羊膜腔内感染越严重，早产发生率越高，并发症出现得也越早 [43]。羊膜腔内感染的高危孕妇不可避免地会早产。因此，患有羊膜内感染的孕妇会在很短的时间后分娩 [44] [48] [49]。目前，没有调查研究或指南规范羊膜内感染或炎症的妇女的靶向干预，也没有适当的评估证明有针对性的产前干预是否会影响新生儿以及结局。

2.12. 细菌性阴道病

孕妇阴道微生物以乳杆菌为主，乳酸杆菌作为抵御生殖道感染的屏障，使阴道环境呈酸性。然而，当乳酸菌的数量急剧下降，厌氧菌增加，从而使阴道微生态紊乱，即细菌性阴道病。研究发现，细菌性阴道病与早产和胎膜早破的发生有关 [50] [51]。因此，产检行阴道分泌物检查是必要的，及时发现并治疗可以改善妊娠结局。

3. 展望

在过去的很长时间，医学的发展在预防母婴重大并发症方面取得了瞩目成就，但降低早产发生率及改善早产孕妇及早产儿结局仍是我国妇幼健康发展的重要目标。随着医学技术的发展及人民认知水平的提高，早产发生率将会逐年降低。

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