

早产人群无症状菌尿的国内外研究进展

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摘 要

新生儿死亡主要原因是早产, 其全球发生率约为12%。泌尿系统感染也是导致孕妇早产及新生儿死亡率增加的一项重要危险因素。多项国际指南均推荐在妊娠期进行ASB合理的筛查及治疗, 进而改善妊娠结局。所以应在不同地区展开临床研究, 收集统计数据分析妊娠期无症状菌尿发生的风险和诊疗方案, 得以建立合理的妊娠期无症状菌尿筛查和治疗方案。本文总结了近些年来无症状菌尿对早产的影响的研究, 以供广大产科同仁参考。

关键词

早产, 无症状菌尿, 孕妇

Research Progress on Asymptomatic Bacteriuria in Premature Populations at Home and Abroad

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Abstract

The primary cause of neonatal death is premature birth, with a global incidence rate of approximately 12%. Urinary tract infections also constitute a significant risk factor contributing to premature birth and increased neonatal mortality rates among pregnant women. Various international guidelines recommend appropriate screening and treatment for asymptomatic bacteriuria (ASB) during pregnancy to improve pregnancy outcomes. Therefore, clinical studies should be conducted in different regions to collect statistical data and analyze the risks and diagnostic and treatment

options for ASB during pregnancy. This approach will enable the establishment of reasonable screening and treatment protocols for ASB in pregnancy. This article summarizes recent research on the impact of asymptomatic bacteriuria on premature birth, serving as a reference for obstetrics professionals.

Keywords

Premature Birth, Asymptomatic Bacteriuria, Pregnant Women

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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。文章显示早产的死亡率为 75% [1]，相较于足月产，早产儿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，有针对性且准确的干预措施能够减少早产的发生[2] [3]。研究表明全球多地早产的发生率高于 10% [2] [4] [5]。随着社会发展，医疗技术及经济水平的提高，目前胎儿存活阈值降低，从而导致早产率明显增加[6] [7]。中国的早产率也居高不下，复旦大学 2012 年中国新生儿协作网的新生儿出生数据显示早产儿约为 10%。多项研究显示妊娠合并无症状菌尿会增加早产的风险[8]，但也有研究认为无症状菌尿与早产的发生无关[9]，目前无症状菌尿与早产之间的关系仍然是一个有争议的问题。妊娠期间筛查 ASB 已成为很多高收入国家的常规产前检查项目[10]-[12]。目前我国多地区已尝试逐步展开妊娠期 ASB 的筛查。

2. 无症状菌尿对早产的影响

2.1. 无症状菌尿(Asymptomatic Bacteriuria, ASB)的定义

没有排尿困难、尿频、尿急、尿痛、耻骨上方疼痛、发热伴膀胱炎症状等泌尿系统感染相关症状，但尿液中可以检测到一种或多种细菌繁殖的状态是诊断 ASB 的必要条件。

2.2. 流行病学

研究显示，在全球范围内，妊娠期 ASB 的发病率在 2%到 10%之间。Stein 等人的文章显示无症状菌尿的发生率与年龄增长呈正相关，15~24 岁的发生率为 2.7%，至 80 岁以上人群发生率增长到 20%~50% [13]。2006 年发表在《美国家庭医生杂志》的文章认为美国孕妇 ASB 的发生率为 1.9%~9.5% [14]。文献报道的不同国家和地区的妊娠期发生率是有很大差异的。2001 年 Smaill 等人报道发达国家和地区妊娠期间 ASB 的发生率为 2%~7% [15]，而来自欠发达地区像尼日利亚(25%~45%)和埃塞俄比亚(21%)的研究显示发生率却高于这个比例[16]。一项针对中国妊娠期 ABS 的研究显示上海地区的妊娠期间 ASB 发生率为 7.7%，新疆地区 ASB 的发生率为 8.2%，作者认为这种差异可能为卫生条件导致或调查人数少导致的统计差异[17]。多项研究显示怀孕并不会增加 ABS 发生率，但近些年发展中国家的孕期 ASB 发生率明显上升[18] [19]。

2.3. ASB 常见菌群及高危因素

ASB 常见的病原体有大肠杆菌、肺炎克雷伯氏菌、奇异变形杆菌和 B 组链球菌。一项研究得出结论，

B 组链球菌的菌落数量增加与绒毛膜羊膜炎的分级增加有关[20]。也有研究表明, B 组链球菌定植与早产的发生呈正相关[21]。因此, B 组链球菌是引起胎儿和母体并发症的最危险的病原体之一。孕期发生 ASB 的危险因素包括产妇年龄小、初产、糖尿病、尿路感染病史、解剖异常、营养不良和社会经济地位低等[22]-[25]。曾有报告显示生殖器卫生为危险因素[26]。

2.4. ASB 的诊断

美国传染病学会(Infectious Disease Society of America, IDSA)确定了 ASB 的细菌学检查标准[27]。此标准为 1956 年 Kass 提出这一诊断标准, 至今一直作为 ASB 诊断的金标准[28]。不论自行留取清洁中段尿, 或通过尿管获取的样本, 需要在连续留取的 2 份尿标本中均分离出同一细菌, 且菌落形成单位 $\geq 10^5$ CFU/ml; 若为单次导尿标本, 尿标本中分离出一种细菌, 菌落形成单位 ≥ 100 CFU/ml。两者满足其一, 则考虑诊断为 ASB。尿液样本留取应尽量避免污染, 并且要在 30 分钟内送检及低温保存[27]。

2.5. 孕期感染 ASB 的风险

由于怀孕期间身体的激素和生理变化, 孕妇更容易感染 ASB。女性较短的尿路和接近肛管的尿路会增加被粪便菌群污染的风险, 再加上怀孕期间免疫力明显下降, 以及 70% 的妇女在怀孕期间出现糖尿, 这就使尿路细菌繁殖有了适宜环境[29]。研究表明, 随着胎龄的增加, 子宫的增大和血清孕酮水平的增加会降低输尿管和膀胱肌的张力, 使其扩张, 从而导致尿滞留。除此之外, 还会出现膀胱尿液反流, 尿液不能完全排出。这些因素促进了妊娠期 ASB 的发生[30]。有研究表明, 大多数患者 ASB 不具有临床意义, 但在孕妇中却相反, 若不予治疗, ASB 发展为急性肾盂肾炎的可能性为 20%~40% [31] [32]。肾盂肾炎中细菌的上升会导致细菌内毒素的释放, 从而启动有毒的炎性细胞因子的释放, 从而导致胎盘的局部循环障碍, 从而影响胎儿, 这会导致中期流产、早产、死产、低出生体重和宫内生长受限[30]。细菌释放的产物, 如粘液酶和促炎毒素, 会分解粘液堵塞, 导致胎膜过早破裂, 这是早产的易感因素[24]。根据世卫组织的说法, 早产是新生儿死亡的主要原因。ASB 是预测早产的重要指标之一。因此, 确定与 ASB 相关的危险因素对于预防胎儿早产将是至关重要的。

2.6. ABS 的治疗

2019 年, 美国预防医学会(United States Preventive Services Task Force, USPSTF)依据系统分析的结果, 推荐对孕妇进行单次尿液培养, 以筛查和治疗 ASB [11]。妊娠期间应用抗生素进行治疗, 除了根据细菌培养结果及药敏试验, 更重要的是胎儿的安全性。治疗妊娠期 ASB 的抗生素可选择头孢菌素类、呋喃妥因或磷霉素。研究显示口服呋喃妥因或磷霉素, 经肾代谢后可以在尿液中有很高的浓度, 治疗 ABS 是有效的, 但是血药浓度相对较低; 同时, 因为呋喃妥因可能增加新生儿黄疸等疾病的风险, 在孕晚期是不建议使用的[10] [11]。多项研究显示呋喃妥因对革兰氏阴性菌和革兰氏阳性菌均敏感[33] [34]。氨苄西林也可以使用, 因为它在怀孕期间更安全, 副作用更小[35] [36]。关于治疗妊娠期 ASB 的疗程选择, 欧洲泌尿外科学会通过 meta 分析和系统综述的形式比较了单疗程给药和短期(2~7 d)给药的疗效和安全性, 结果发现在预防后续泌尿系统感染方面没有差异, 早产的发生率也没有明显差异。但单次疗程给药者分娩低出生体重儿的风险增高, 因此推荐 2~7 d 短期给药方案。在进行 1 个疗程治疗后, 建议间隔 1~2 周再进行 1 次尿液培养, 若仍存在 ASB, 可再次给予单次治疗, 疗程可延长至 10~14 d [37]。Rotjanapan 等人对患有 ABS 的患者进行不规范的抗生素治疗发现, 不规范治疗组有 12% 出现了难治性梭状芽孢杆菌感染, 其发生率是未使用抗生素组的 8 倍[38]。所以, 如果对 ABS 不加选择地进行治疗, 非但不获益, 反而可能增加耐药菌感染风险, 尤其是对于妊娠女性, 规范、合理的治疗能够减少 ASB 对孕妇及胎儿的影响。

3. 展望

目前 ASB 与早产存在一定的相关性,但相关证据质量参差不齐,仍存在一定的争议,还需高质量的前瞻性随机调查研究证实其相关性。多数研究支持在妊娠早期对 ASB 进行筛查和治疗,以降低妊娠并发症的风险。同时抗生素耐药性问题也需要进一步的研究来优化治疗策略,并为有效的预防指明方向。

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