

·生殖道沙眼衣原体感染·综述·

生殖道沙眼衣原体感染的不良妊娠及生育结局

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王洪琳和翁榕星对本文有同等贡献

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【摘要】 近年来全球生殖道沙眼衣原体感染病例攀升, 该感染的隐匿性导致部分患者难以被发现、诊断和及时治疗, 不及时治疗可能导致不孕不育、异位妊娠、自然流产、早产等严重的不良妊娠及生育结局, 影响优生优育和生殖健康水平。本文对目前生殖道沙眼衣原体感染导致不良妊娠及生育结局的现状, 及其致病机制、结局种类和预防措施等作一综述。

【关键词】 衣原体, 沙眼; 不良妊娠; 不孕不育; 自然流产; 早产

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Adverse effects of *Chlamydia trachomatis* infection on pregnancy and reproductive outcomes

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【Abstract】 The incidence of *Chlamydia trachomatis* (CT) infection has increased rapidly worldwide. Many CT infection cases are asymptomatic that leads to a missed opportunity to prevent CT infection through detection and treatment. Untreated CT infection may cause adverse pregnancy and reproductive outcomes including infertility, ectopic pregnancy, spontaneous abortion, preterm labor, which will affect eugenics and reproductive health. In this review, the current situation of adverse pregnancy and reproductive outcomes caused by CT infection, pathogenic mechanism, types of outcomes and preventive measures are summarized.

【Key words】 *Chlamydia trachomatis*; Adverse pregnancy outcome; Infertility; Spontaneous abortion; Preterm labor

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生殖道沙眼衣原体(*Chlamydia trachomatis*, CT)感染是全球范围内最常见的性传播感染之一^[1],我国近年来报告病例数亦明显增加^[2]。感染者中有约 70%的女性和 50%的男性表现为无症状,若不能得到及时有效治疗,可能导致严重的不良妊娠及生育结局^[3]。本文基于目前生殖道 CT 感染导致不良

妊娠及生育结局的现状,针对致病机制、结局种类、预防进展等进行综述,以期今后我国开展相关研究提供科学依据。

一、CT 感染导致泌尿生殖道系统损害的机制

CT 感染宿主后,既为宿主提供了免疫防御与抵抗,也会造成免疫损伤,是 CT 致病的主要原因^[4]。研究表明,当机体抵

抗力下降时,CT 侵入柱状上皮,可引起宫颈炎和子宫内膜炎^[5],通过上行感染引起输卵管等部位感染,甚至导致输卵管扭曲、黏连、堵塞,致使异位妊娠或不孕不育^[6],究其原因,一方面,CT 可以通过黏附到生殖上皮细胞表面溶解其膜磷脂,直接损伤生殖道的上皮细胞进而引起组织的粘连等损害,CT 的生长代谢也可以产生大量氨气,破坏宿主细胞,造成组织损伤和炎症反应^[7];另一方面,CT 也可以通过迟发型超敏反应和诱导自身免疫应答造成组织损伤^[8]。CT 抗原热休克蛋白 HSP60 和人体组织细胞存在交叉,当机体免疫系统识别衣原体 HSP60 时,也会导致自体细胞被 Th1 细胞、多形核白细胞和 NK 细胞等免疫细胞以及特异性抗体攻击,导致炎症因子 IL-8、IL-6、TNF- α 、生长因子血管内皮生长因子(VEGF)与表皮生长因子(EGF)的升高,进一步加重炎症反应,造成组织的损伤、重塑、纤维化和瘢痕形成^[9]。有研究表明,CT 的持续感染会导致子宫内膜出现淋巴细胞和巨噬细胞的浸润产生慢性炎症反应,激活杀伤 T 细胞,诱发自身免疫反应和细胞凋亡,促使各种炎症因子产生,干扰胚胎着床,导致不孕;也可使生长中的胚胎受到干扰,造成早期流产^[10]。此外,CT 释放的内毒素会破坏精子形态,使精子内膜受损,影响精子活力,降低精卵结合机会^[11]。

二、生殖道 CT 感染与不良妊娠及生育结局

1. 不孕不育

女性感染生殖道 CT 后,可导致宫颈炎、尿道炎,并沿生殖道上行感染导致子宫内膜炎、输卵管炎、慢性盆腔炎等^[12]。约 20% 的女性 CT 感染者会发生慢性盆腔炎,是诱发患者慢性盆腔痛、输卵管性不孕不育的重要危险因素^[12],在丹麦的一项大型回顾性人群队列研究发现,有过 CT 感染的女性有较高的输卵管不孕发生风险^[13]。鉴于生殖道 CT 感染者中女性无症状感染者比例高达 70%^[14],早期筛查和治疗 CT 感染是预防女性不孕症的关键措施。

男性感染生殖道 CT 后,若未经早期规范治疗,会发生尿道炎和附睾炎^[14],这些感染可能导致梗阻性无精子症^[15],或造成精子数量下降^[16]。体外实验也证实 CT 感染可促进精子细胞的凋亡,增加精子中的 DNA 碎片,造成无精症、少精症、弱精症等男方因素导致不孕的风险^[7]。

2. 异位妊娠

异位妊娠指受精卵在子宫腔外着床发育的异常妊娠过程,其可能伴随着输卵管破裂和出血等相关并发症,并且是导致孕妇死亡的重要原因,研究发现生殖道感染会让异位妊娠发生风险增加 3~4 倍^[17]。发生异位妊娠的孕妇 CT 感染率在 21%~60%,而未发生异位妊娠的孕妇 CT 感染率在 15%~26%^[18-20]。丹麦的研究也发现,有着一次或以上 CT 感染的女

性有较高的异位妊娠发生风险^[13]。中国的研究也指出 CT 感染史是发生异位妊娠的危险因素之一^[21],另一项研究发现 CT 血清学 IgG 检测阳性是发生异位妊娠的危险因素之一^[22]。病例对照研究和队列研究合并效应量均显示 CT 感染与异位妊娠存在显著性相关^[3]。

3. 自然流产

生殖道感染包括 CT 感染被认为是流产的潜在诱因。伊朗一项研究发现有自然流产史的孕妇 CT 患病率显著高于正常生产的孕妇^[23],且 CT DNA 在流产女性的受孕产物和胎盘中更为常见^[24]。

4. 死产

CT 感染也可能导致死产,例如,有研究发现发生死产的产妇中约 33.3% 有 CT 抗体,而活产产妇中约 10.4% 有 CT 抗体^[25]。近年关于 CT 感染与死产的相关性研究相对较少,值得注意的是,在澳大利亚针对不同地区人群的 2 项队列研究中发现不同的结果,新南威尔士的队列研究表明产前 CT 感染会显著性增加死产的风险^[26],但是在西悉尼的研究指出 CT 感染与死产并无显著性相关^[27]。

5. 早产

有研究显示有症状的生殖道 CT 感染及其导致的慢性宫颈炎是早产的危险因素^[28]。早期筛查以及治疗 CT 感染可显著降低孕妇发生早产的风险^[29]。但也有一些研究表明生殖道 CT 感染与早产没有相关性^[30]。

6. 其他不良妊娠结局

CT 感染对其他不良结局如低出生体重、先兆子痫等影响的研究较少,且尚存有争议。美国一项研究发现,CT 感染显著增加新生儿低出生体重的风险^[31],但是在另外数项队列研究中 CT 感染与低出生体重并无显著性相关^[32-33]。CT 感染与先兆子痫方面,美国的研究发现 CT 感染显著增加发生先兆子痫的风险($aOR=7.2, 95\%CI: 1.3\sim 39.7$),而丹麦的研究显示 CT 感染与先兆子痫并无显著性相关^[34]。有报告指出约 25% 的宫内生长受限新生儿的胎盘中检测出 CT^[35],但是在澳大利亚的一项超过 10 万人的大型队列研究显示,CT 感染与宫内生长受限并无显著性相关^[27]。

三、预防生殖道 CT 感染致不良妊娠与生育结局的措施

生殖道 CT 感染和其他性传播疾病可通过产前筛查得到预防,从而降低妊娠和新生儿并发症的发生^[36]。全球多个国家已开展普通人群的生殖道 CT 筛查:美国预防服务工作组于 2001 年发布公告,强烈建议临床医生对 25 岁以下的年轻女性或者是 25 岁以上无症状但有潜在生殖道 CT 感染风险的女性(如更换性伴等)进行常规的 CT 检测^[37];英国自 2002 年 9 月开始对 25 岁以下的青年人群提供 CT 筛查服务^[38]。因此,

早期筛查和治疗生殖道 CT 感染是控制疾病传播,减少并发症,降低感染所导致不良妊娠及生育结局的关键措施。

四、结语

近年来全球生殖道 CT 感染病例数攀升,其对妊娠和生育的影响可能演变成严峻的全球性公共卫生问题。CT 感染可能导致不良妊娠及生育结局,也可能对低出生体重、宫内生长受限以及先兆子痫有一定影响,应当重视不良妊娠及生育结局的早期预警和干预,可将产前筛查 CT 和淋病奈瑟菌感染等性传播感染与目前成功实施的艾滋病和梅毒的产前筛查相关网络结合起来,有关筛查和治疗等措施是否可以改善妊娠及生育结局以及其所能带来的成本效益等方面的研究也有待加强,以期为决策者制定针对我国人群的策略提供依据。

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