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女性生殖道解脲支原体感染与胎膜早破与新生儿窒息的相关性 *

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摘要 目的：探讨女性生殖道解脲支原体(Ureaplasma urealyticum，UU)感染与胎膜早破与新生儿窒息的相关性。**方法：**2017 年 6 月至 2019 年 6 月选择在地区门诊就诊的孕妇 108 例，检测生殖道解脲支原体感染情况，调查所有孕妇的一般资料、分娩方式、胎膜早破、新生儿窒息状况并进行相关性分析。**结果：**在 108 例孕妇中，48 例检出解脲支原体感染，感染率为 44.4 %。感染组的年龄、体重指数、产次、孕次、受教育年限、孕周等与非感染组对比差异无统计学意义(P>0.05)。感染组的胎膜早破与新生儿窒息发生率分别为 22.9 %和 18.8 %，显著高于非感染组的 3.3 %和 1.7 %(P<0.05)。感染组的剖宫产率高于非感染组，自然分娩率低于非感染组，对比差异都有统计学意义 (P<0.05)。在 108 例孕妇中，Pearson 分析显示解脲支原体感染与胎膜早破、新生儿窒息都存在相关性(P<0.05)。**结论：**女性生殖道解脲支原体感染比较常见，可导致剖宫产、胎膜早破、新生儿窒息发生率增加，也与胎膜早破、新生儿窒息存在显著相关性。

关键词：女性生殖道；解脲支原体感染；剖宫产；胎膜早破；新生儿窒息

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Correlation between Female Genital Tract Ureaplasma Urealyticum Infection and Premature Rupture of Membranes and Neonatal Asphyxia*

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ABSTRACT Objective: To explore the correlation between female genital tract Ureaplasma urealyticum (Ureaplasma urealyticum, UU) infection and premature rupture of membranes and neonatal asphyxia. **Methods:** From June 2017 to June 2019, 108 cases of pregnant women who were selected as outpatients in the region were selected, all the cases were to detect the genital tract Ureaplasma urealyticum infection. The general information, delivery methods, premature rupture of membranes, and neonatal asphyxia were investigated for all pregnant women and were given correlation analysis. **Results:** There were 48 cases were detected Ureaplasma urealyticum infection in the 108 cases that the infection rates were 44.4 %. There were no significant difference in age, body mass index, parity, pregnancy time, years of education, and gestational age compared between the infected group and the non-infected group (P>0.05). The incidences of premature rupture of membranes and neonatal asphyxia in the infected group were 22.9 % and 18.8 %, respectively, which were significantly higher than that in the non-infected group of 3.3 % and 1.7 %(P<0.05). The cesarean section rates in the infected group were higher than that in the non-infected group, and the natural delivery rate were lower than that in the non-infected group that compared the differences were statistically significant(P<0.05). In the 108 pregnant women, Pearson analysis showed that Ureaplasma urealyticum infection were associated with premature rupture of membranes and neonatal asphyxia(P<0.05). **Conclusion:** Ureaplasma urealyticum infection in female genital tract is relatively common, which can lead to an increase in the incidence of cesarean section, premature rupture of membranes, and neonatal asphyxia. It is also significantly associated with premature rupture of membranes and neonatal asphyxia.

Key words: Female reproductive tract; Ureaplasma urealyticum infection; Cesarean section; Premature rupture of membranes; Neonatal asphyxia

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前言

解脲支原体(Ureaplasma urealyticum,UU)是人类泌尿生殖道常见的微生物,在自然界中分布广泛,只有少数可引起人和动物感染,多数为不致病性[1,2]。其为一种特殊的病原体,无细胞壁,大小处于细菌和病菌之间。解脲支原体可通过垂直传播方式侵入体内,改变宫颈粘液 pH 值,从而诱发盆腔炎、子宫内膜炎、输卵管炎、不孕等疾病的发生[3,4]。并且解脲支原体有超抗原作用,可激活 T 淋巴细胞及巨噬细胞,引起受感染部位免疫功能紊乱,可直接诱发细胞凋亡,释放大量细胞因子,引起组织病理损伤[5]。研究表明新生儿主要是通过产道感染这种解脲支原体,育龄妇女生殖道携带解脲支原体是引起新生儿和围生期妇女侵袭性感染的直接原因[6,7]。比如胎膜早破可导致新生儿在通过产道时接触解脲支原体,造成新生儿宫内感染[8,9]。研究表明约 25 %孕妇生殖道内有解脲支原体感染,其中约 1/2 的感染者可感染给新生儿,引起早产、胎儿窘迫、新生儿窒息等情况的发生[10,11]。本文具体调查了本地区女性生殖道解脲支原体感染,分析了女性生殖道解脲支原体感染与胎膜早破、新生儿窒息的相关性,希望提高本地区广大妊娠期妇女的健康水平,为解脲支原体感染预防措施的制定提供依据。现总结报道如下。

1 材料与方法

1.1 研究对象

2017 年 6 月至 2019 年 6 月选择在地区门诊就诊的孕妇 108 例,纳入标准:单胎,孕周≥ 12 w;年龄 20~45 岁;孕妇在知情背景下自愿签署了同意书; 医院伦理委员会批准了此次研究;取材前 1 w 均没有使用过抗生素,并且最近 1 周没有性交史。排除标准:近 1 w 内有性生活及阴道用药、灌洗史或应用抗生素及激素类药物;存在头盆不称的产妇;临床资料缺乏者;合并妊娠期高血压疾病、妊娠期糖尿病等疾病的产妇;孕妇在孕期吸烟、喝酒、吸毒等不良习惯。

1.2 解脲支原体感染检测

擦去所有孕妇的外阴分泌物,无菌窥器暴露阴道,用无菌棉签拭子(诸暨市德凌生化有限公司生产)置于宫颈管内约 2 cm 处并旋转 6~8 w, 拭子放入无菌试管中立即送解脲支原体培养。解脲支原体培养基购自郑州博赛生物工程公司,37℃恒温箱培养 24~28 h,培养基颜色不变或明显混浊变红判断为阴性,培养基颜色由黄变红而且清澈透明为阳性。

1.3 临床资料调查

(1)调查所有孕妇的产次、孕次、年龄、孕周等指标。(2)记录孕妇的胎膜早破与新生儿窒息发生情况。胎膜早破诊断标准:临床特征:窥开阴道见液体自宫口流出,孕妇突感有液体自阴道流出。辅助检查特征:阴道液涂片检查可见羊齿植物叶状结晶,阴道液 pH 值≥ 6.5。新生儿窒息程度:1 min APgar 评分≤ 7 分。(3)记录所有孕妇的分娩预后,包括自然分娩、阴道助产与剖宫产。

1.4 统计方法

用 Excel 建立数据资料库,选择 SPSS22.00 软件对本研究所有数据进行分析与处理,计量数据与计数数据采用均数± 标准差、%等表示,对比方法为 t 检验、卡方 x^2 分析,相关性分析采用 Pearson 分析,以 P<0.05 为差异有统计学意义。

2 结果

2.1 解脲支原体感染情况

在 108 例孕妇中,48 例检出解脲支原体感染, 感染率为 44.4 %。

2.2 一般资料对比

感染组的年龄、体重指数、产次、孕次、受教育年限、孕周等与非感染组对比差异无统计学意义(P>0.05),见表 1。

表 1 两组一般资料对比($\bar{x}\pm s$)

Table 1 Comparison of two sets of general information ($\bar{x}\pm s$)

Groups	n	Age(years)	BMI(kg/m^2)	Parity (times)	Pregnancy times (times)	Years of education (years)	Gestational week (weeks)
Infection group	48	27.39± 2.49	22.79± 2.14	1.89± 0.37	2.11± 0.38	14.59± 2.14	25.14± 0.56
Non-infected group	60	27.09± 2.11	22.88± 1.45	1.81± 0.42	2.02± 0.37	14.38± 3.11	25.22± 0.61

2.3 胎膜早破与新生儿窒息发生情况对比

感染组的胎膜早破与新生儿窒息发生率分别为 22.9 %和 18.8 %,显著高于非感染组的 3.3 %和 1.7 %(P>0.05),见表 2。

表 2 组胎膜早破与新生儿窒息发生情况对比(例,%)

Table 2 Comparison of premature rupture of membranes and neonatal asphyxia (n,%)

Groups	n	Premature rupture of membranes	Neonatal asphyxia
Infection group	48	11(22.9)*	9(18.8)*
Non-infected group	60	2(3.3)	1(1.7)

Note: Compared with the non-infected group, *P<0.05.

2.4 分娩方式对比

感染组的剖宫产率高于非感染组,自然分娩率低于非感染组,对比差异都有统计学意义(P<0.05),见表 3。

2.5 相关性分析

在 108 例孕妇中,Pearson 分析显示解脲支原体感染与胎膜早破、新生儿窒息都存在相关性(P<0.05),见表 4。

表 3 两组分娩方式对比(例,%)

Table 3 Comparison of delivery methods between two groups (n,%)

Groups	n	Cesarean section	Vaginal midwifery	Natural delivery
Infection group	48	30(62.5)*	6(12.5)	12(25.0)*
Non-infected group	60	12(20.0)	9(15.0)	39(65.0)

Note: Compared with the non-infected group, *P<0.05.

表 4 女性生殖道解脲支原体感染与胎膜早破、新生儿窒息的相关性(n=108)

Table 4 Correlation between female genital tract Ureaplasma urealyticum infection and premature rupture of membranes and neonatal asphyxia (n=108)

Index	Premature rupture of membranes	Neonatal asphyxia
r	0.563	0.744
P	0.003	0.000

3 讨论

生殖道感染是孕妇常见病，主要包括解脲支原体阴道炎、支原体阴道炎、假丝酵母菌阴道炎、滴虫性阴道炎、细菌性阴道病等[12,13]。妇女阴道菌群包括乳酸杆菌、支原体阴道炎、假丝酵母菌、解脲支原体、肺炎克雷伯杆菌、变形杆菌、B 族链球菌等[14]，正常情况下各菌群和宿主、环境之间构成相互制约，从而可建立起阴道微生态环境[15,16]。解脲支原体是一种支原体，外表无细胞壁，能破坏宿主细胞上的磷脂，破坏机体微生态，损伤宿主组织器官，能使花生四烯酸转变为前列腺素，从而促进机体发生炎性反应，导致子宫收缩[17,18]。本研究显示在 108 例孕妇中，48 例检出解脲支原体感染，感染率为 44.4 %，表明女性生殖道普遍存在解脲支原体感染。

解脲支原体黏附于宿主细胞表面，定居在泌尿生殖道上皮细胞，从宿主细胞膜吸取脂质，产生毒性代谢产物，引起细胞膜损伤，导致机体局部免疫功能下降，可影响宿主细胞的生物合成[19]。胎膜早破是指妊娠胎膜在临产前发生破裂，导致胎膜早破的最主要的原因是感染[20]。已有研究表明解脲支原体感染可导致胎膜早破、绒毛膜羊膜炎、死胎等并发症的发生，严重影响母儿预后[21,22]。并且解脲支原体感染可以通过垂直传播方式传给胎儿，其作为一种条件致病菌，妊娠期感染后可引起新生儿窒息、早产、胎儿窘迫的发生[23]。有研究表明解脲支原体感染阳性组的孕妇，早产、新生儿窒息、胎儿窘迫的发生率显著高于阴性者，多种病原体联合感染比单种病原体感染母婴垂直传播率高[24,25]。本研究显示感染组的胎膜早破与新生儿窒息发生率分别为 22.9 %和 18.8 %，显著高于非感染组的 3.3 %和 1.7 %。本研究的结果与梁媛[26]等的研究类似，该学者对 327 例分娩产妇进行产前宫颈分泌物解脲支原体检测，98 例检出解脲支原体感染，感染率为 29.97 %，且感染组患者早产的发生率 19.39 %和胎膜早破的发生率 35.71 %，均高于非感染组的 6.99 %、13.97 %，同时该学者也发现感染组患者发生低出生体重儿的发生率为 10.20 %，新生儿黄疸发生率为 14.29 %，新生儿肺炎发生率为 9.18 %，均高于非感染组的 4.37 %、6.11 %、2.62 %，从机制上分析，解脲支原体对机体具有直接损伤作用，刺激宿主免疫活性细胞产生释放多种细胞因子，从而破坏宿主细胞，损伤器官组织，影响蛋白质和 DNA 合成，导致新生儿窒息的发生[27]。同时解脲支原体也可破坏细胞内的酸性环境，造成溶酶体酶不稳定，可减少宫颈的免疫球蛋白的活性，继而释放前列腺素，从而导致胎膜早破的发生。解脲支原体为泌尿生殖道感染的常见病原体，也是一种原核细胞型微生物。解脲支原体感染与流产、早产、胎膜早破、新生儿疾病等有一定的相关性[28]。本研究显示感染组的剖宫产率高于非感染组，自然分娩率低于非感染组，与王利娟[29]的研究一致，通过探究育龄妇女妊娠期解脲支原体感染与妊娠结局的关系，发现解脲支原体感染患者剖宫产率高于解脲支原体携带患者和非感染患者，不良妊娠结局发生率也显著升高，而解脲支原体携带患者和非感染患者无差异性，说明育龄妇女妊娠期解脲支原体感染是影响不良妊娠结局的一个重要因素。从机制上分析，解脲支原体可上行感染胎膜、羊水、胎盘，使胎盘供给胎儿的氧与营养物质输送障碍，影响胎儿发育，引起胎儿宫内生长受限。并且解脲支原体可使新生儿呼吸道纤毛运动受到影响，可引起局部环境 pH 值的改变，促进其他病原体的生长繁殖，从而增加剖宫产发生几率[30,31]。

解脲支原体是引起围生期感染的重要病原体，可使得孕妇阴道内乳酸杆菌减少，而厌氧菌、革兰阴性杆菌增多，可降解胎膜的基质及胶质，直接影响胎膜的弹性和强度，从而导致胎膜早破的发生[32]。并且解脲支原体产生的尿素酶等毒性物质，促进其他病原体的生长繁殖，使胎膜的张力下降，直接引起胎膜损伤[33]。本研究 Pearson 分析显示女性生殖道解脲支原体感染与胎膜早破、新生儿窒息都存在相关性，与刘文静[34]等人的研究类似，发现生殖道感染与早产、低体重新生儿、新生儿窒息、新生儿感染、胎膜早破、早产胎膜早破、绒毛膜羊膜炎、死胎等均相关。因此女性生殖道解脲支原体感染会严重影响了母婴的生命安全，需引起高度关注。本研究也存在一定的不足，调查的孕妇人数比较少，且没有进行长期跟踪随访分析，将在后续研究中深入探讨。

总之，女性生殖道解脲支原体感染比较常见，可导致剖宫产、胎膜早破、新生儿窒息发生率增加，也与胎膜早破、新生儿窒息存在显著相关性。

参 考 文 献(References)

[1] 朱云,贾雪梅.β-HCG、PROG、E2 及 CA125 在先兆流产中的临床检测意义[J].川北医学院学报, 2019, 34(4): 441-444

[2] 杜娟,夏敏.多因素 Logistic 回归分析稽留流产的危险因素[J].川北医学院学报, 2019, 34(5): 608-611

[3] Silwedel C, Haarmann A, Fehrholz M, et al. More than just inflammation: Ureaplasma species induce apoptosis in human brain microvascular endothelial cells[J]. J Neuroinflammation, 2019, 16(1): e38

[4] Silwedel C, Speer CP, Haarmann A, et al. Ureaplasma Species Modulate Cytokine and Chemokine Responses in Human Brain Microvascular Endothelial Cells[J]. Transpl Infect Dis, 2019, 20(14): 789-792

[5] Silwedel C, Speer CP, Haarmann A, et al. Ureaplasma species modulate cell adhesion molecules and growth factors in human brain microvascular endothelial cells [J]. World J Mens Health, 2019, 121(9): e154737

[6] Smith M, Crews JD, Cheek N, et al. Hyperammonemic Encephalopathy due to Ureaplasma parvum Infection in an Immunocompromised Child[J]. Pediatrics, 2019, 144(2): 114-119

[7] Claus H, Schlegel N, Glaser K, et al. Classification of non-gonococcal urethritis: a review[J]. Int J Mol Sci, 2019, 51(6): 901-907

[8] Feriyawati L, Anggraini DR, Nasution TA. Co-Infection of Human Papillomavirus with Mycoplasma Hominis/Ureaplasma Urealyticum Among Female Sex Workers in Medan, Indonesia [J]. Open Access Maced J Med Sci, 2019, 7(20): 3425-3428

[9] Glaser K, Gradzka-Luczewska A, Szymankiewicz-Breborowicz M, et al. Perinatal Ureaplasma Exposure Is Associated With Increased Risk of Late Onset Sepsis and Imbalanced Inflammation in Preterm Infants and May Add to Lung Injury[J]. Front Cell Infect Microbiol, 2019, 9: e68

[10] Jang YS, Min JW, Kim YS. Positive culture rate and antimicrobial susceptibilities of Mycoplasma hominis and Ureaplasma urealyticum [J]. Obstet Gynecol Sci, 2019, 62(2): 127-133

[11] Kaestner S, Thomé M, Stuebinger K, et al. Possible shunt infection with Ureaplasma urealyticum in an ELBW preterm [J]. Childs Nerv Syst, 2019, 35(12): 2253-2254

[12] Kukul E, Song T. Detection of Ureaplasma spp. serovars in genital tract of infertile males[J]. Int Urol Nephrol, 2019, 33(5): e22865

[13] Kusanovic JP, Vargas P, Ferrer F, et al. Comparison of two identification and susceptibility test kits for Ureaplasma spp and Mycoplasma hominis in amniotic fluid of patients at high risk for intra-amniotic infection[J]. J Matern Fetal Neonatal Med, 2019, 20: 1-9

[14] Beeton ML, Payne MS, Jones L. The Role of Ureaplasma spp. in the Development of Nongonococcal Urethritis and Infertility among Men [J]. Clin Microbiol Rev, 2019, 32(4): 99-104

[15] Cai S, Pan J, Duan D, et al. Prevalence of Ureaplasma urealyticum, Chlamydia trachomatis, and Neisseria gonorrhoeae in gynecological outpatients, Taizhou, China[J]. J Clin Lab Anal, 2020, 34(2): e23072

[16] Valentine-King MA, Cisneros K, James MO, et al. Turning the Tide against Antibiotic Resistance by Evaluating Novel, Halogenated Phenazine, Quinoline, and NH125 Compounds against Ureaplasma Species Clinical Isolates and Mycoplasma Type Strains [J]. Antimicrob Agents Chemother, 2019, 63(3): 221-224

[17] Veiga E, Treviño M, Romay AB, et al. Prevalence of genital Mycoplasma and response to eradication treatment in patients undergoing assisted reproductive techniques[J]. Infect Agent Cancer, 2019, 32 (4): 327-332

[18] Zou J, Pichon M, Gebeile R, et al. Which sample for the transport of mycoplasma, eSwab® or dry swab?[J]. J Clin Lab Anal, 2019, 77(1): 95-98

[19] Cavanagh M, Amabebe E, Anumba DOC. Differential cytokine and metabolite production by cervicovaginal epithelial cells infected with Lactobacillus crispatus and Ureaplasma urealyticum [J]. Anaerobe, 2020, 62(14): e102101

[20] Liang Y, Chen M, Qin L, et al. A meta-analysis of the relationship between vaginal microecology, human papillomavirus infection and cervical intraepithelial neoplasia[J]. Infect Agent Cancer, 2019, 14: e29

[21] Liu Z, Zhang Y, Han Y, et al. The Results of Three-Year Monitoring of Mycoplasma Hominis and Ureaplasma Urealyticum in the Cantons of Herzegovina-Neretva and West Herzegovina [J]. J Clin Lab Anal, 2019, 31(Suppl 1): 131-132

[22] Moragianni D, Dryllis G, Andromidas P, et al. Genital tract infection and associated factors affect the reproductive outcome in fertile females and females undergoing in vitro fertilization [J]. Biomed Rep, 2019, 10(4): 231-237

[23] Noh EJ, Kim DJ, Lee JY, et al. Ureaplasma Urealyticum Infection Contributes to the Development of Pelvic Endometriosis Through Toll-Like Receptor 2[J]. Front Immunol, 2019, 10(15): e2373

[24] Nowbakht C, Edwards AR, Rodriguez-Buritica DF, et al. Two Cases of Fatal Hyperammonemia Syndrome due to Mycoplasma hominis and Ureaplasma urealyticum in Immunocompromised Patients Outside Lung Transplant Recipients [J]. Antimicrob Agents Chemother, 2019, 6(3): ofz033

[25] Park H, Lee G. Roles of Ureaplasma Species in Idiopathic Chronic Prostatitis: A Case-Control Study [J]. World J Mens Health, 2019, 37 (3): 355-363

[26] 梁媛, 刘洁玲, 占晓兰,等. 解脲支原体感染孕妇对妊娠结局影响与预防措施分析[J].中华医院感染学杂志, 2018, 28(23): 3640-3642, 3646

[27] Rittenschober-Böhm J, Waldhoer T, Schulz S M, et al. Vaginal Ureaplasma parvum serovars and spontaneous preterm birth[J]. Am J Obstet Gynecol, 2019, 220(6): 594.e1-594.e9

[28] Rouard C, Pereyre S, Abgrall S, et al. Early prosthetic joint infection due to Ureaplasma urealyticum: Benefit of 16S rRNA gene sequence analysis for diagnosis [J]. J Microbiol Immunol Infect, 2019, 52(1): 167-169

[29] 王利娟. 育龄妇女妊娠期解脲支原体感染与妊娠结局关系分析[J]. 现代诊断与治疗, 2018, 29(19): 3106-3107

[30] Rumyantseva T, Khayrullina G, Guschin A, et al. Prevalence of Ureaplasma spp. and Mycoplasma hominis in healthy women and patients with flora alterations [J]. Diagn Microbiol Infect Dis, 2019, 93 (3): 227-231

[31] Schwartz DJ, Elward A, Storch GA, et al. Ureaplasma urealyticum pyelonephritis presenting with progressive dysuria, renal failure, and neurologic symptoms in an immunocompromised patient [J]. Transpl Infect Dis, 2019, 21(2): e13032

[32] Silwedel C, Fehrholz M, Speer CP, et al. Differential modulation of pulmonary caspases: Is this the key to Ureaplasma-driven chronic inflammation?[J]. PLoS One, 2019, 14(5): e0216569

[33] Totten AH, Crawford CL, Dalecki AG, et al. Differential Susceptibility of Mycoplasma and Ureaplasma Species to Compound-Enhanced Copper Toxicity[J]. Front Microbiol, 2019, 10(8): e1720

[34] 刘文静, 林秋婵, 关咏超, 等.妊娠期生殖道感染的相关因素及妊娠结局分析[J].中国性科学, 2018, 27(3): 122-125