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在线全文

高龄复发性流产患者体液免疫异常的单中心研究*

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【摘要】 **目的** 探讨高龄复发性流产（recurrent spontaneous abortion, RSA）患者体液免疫状态。**方法** 采用回顾性研究方法，纳入2022年1月–2023年10月在本中心就诊的RSA患者，检测其多种自身抗体，采用多因素logistic回归方法，在控制体质量指数（body mass index, BMI）、既往活产史、自然流产次数三个混杂因素的基础上，比较不同年龄分组（低龄组20～34岁，高龄组35～45岁）与多种自身抗体之间的关联，进而探讨高龄RSA女性与低龄RSA女性体液免疫状态差异。**结果** 共纳入4 008例RSA女性，其中高龄组1 158例，低龄组2 851例。高龄组和低龄组抗磷脂综合征、系统性红斑狼疮、干燥综合征、类风湿性关节炎、未分化结缔组织病的患病率分别为15.6%和14.1%、0.0%和0.1%、0.9%和0.9%、0.3%和0.0%、23.7%和22.6%，两组比较差异无统计学意义。高龄组和低龄组抗磷脂抗体（antiphospholipid antibodies, aPLs）阳性率分别为19.1%和19.5%，抗核抗体（antinuclear antibody, ANA）阳性率分别为6.6%和6.6%，抗可提取核抗原（extractable nuclear antigen, ENA）抗体阳性率分别为9.2%和10.5%，抗双链DNA（anti-double stranded DNA, dsDNA）抗体阳性率分别为2.0%和2.0%，抗单链DNA（anti-single-stranded DNA, ssDNA）抗体阳性率分别为2.2%和1.2%，抗α-胞衬蛋白抗体（antibodies against alpha-fodrin, AAA）阳性率分别为5.1%和4.9%，甲状腺自身免疫（thyroid autoimmunity, TAI）分别为17.8%和16.8%，两组比较差异均无统计学意义，高龄组中狼疮抗凝物（lupus anticoagulant, LA）阳性率为1.6%，低龄组为2.7%，差异有统计学意义（校正的优势比=0.36，95%置信区间：0.17～0.78）。4 008例RSA患者中aPLs谱中三种抗体累计阳性778例，其中抗β2糖蛋白Ⅰ抗体（anti-β2 glycoprotein Ⅰ antibodies, β2GPⅠAb）-IgG/IgM阳性者520例，aCL-IgG/IgM阳性者58例，LA阳性者73例，β2GPⅠAb-IgG/IgM与aCL-IgG/IgM同时阳性者105例，β2GPⅠAb-IgG/IgM与LA同时阳性者17例，aCL-IgG/IgM与LA同时阳性者2例，三种抗体均阳性者3例。**结论** 本研究未发现高龄RSA患者与低龄RSA患者体液免疫状态存在差异。

【关键词】 高龄 复发性流产 体液免疫

Humoral Immunity Abnormalities in Advanced Maternal-Age Women With Recurrent Spontaneous Abortion: A Single Center Study

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【**Abstract**】 **Objective** To determine the humoral immunity in advanced maternal-age women with recurrent spontaneous abortion (RSA). **Methods** A retrospective study was performed between January 2022 and October 2023 in the Department of Reproductive Immunity of Shanghai First Maternity and Infant Hospital. Women with RSA were recruited and multiple autoantibodies were tested. Multivariate logistic regression was performed to compare the associations between different age groups (20 to 34 years old in the low maternal-age group and 35 to 45 years in the advanced maternal-age group) and multiple autoantibodies, while controlling for three confounding factors, including body mass index (BMI), previous history of live birth, and the number of spontaneous abortions. Then, we investigated the differences in the humoral immunity of advanced maternal-age RSA women and low maternal-age RSA women. **Result** A total of 4 009 women with RSA were covered in the study. Among them, 1 158 women were in the advanced maternal-age group and 2 851 women were in the low maternal-age group. The prevalence of antiphospholipid syndrome, systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, and undifferentiated connective tissue disease was 15.6% and 14.1%, 0.0% and 0.1%, 0.9% and 0.9%, 0.3% and 0.0%, and 23.7% and 22.6% in the advanced maternal-age group and low maternal-age group, respectively, showing no statistical difference between the two groups. The positive rates of antiphospholipid antibodies (aPLs), antinuclear antibody (ANA), extractable nuclear antigen (ENA) antibody, anti-double stranded DNA (dsDNA) antibody, anti single-stranded DNA (ssDAN) antibody, antibodies against alpha-fodrin (AAA), and thyroid autoimmunity (TAI) were 19.1% and 19.5%, 6.6% and 6.6%, 9.2% and 10.5%, 2.0% and 2.0%, 2.2% and 1.2%, 5.1% and 4.9%, and 17.8% and 16.8%, respectively. No differences were observed between the two groups. 1.6% of the women in the advanced maternal-age group tested positive for lupus anticoagulant (LA), while 2.7% of the women in the low maternal-age group were LA positive, with the differences being statistically significant (odds

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ratio=0.36, 95% confidence interval: 0.17-0.78). In the 4008 RSA patients, the cumulative cases tested positive for the three antibodies of the aPLs spectrum were 778, of which 520 cases were positive for anti-β2 glycoprotein Ⅰ antibodies (β2GPⅠ Ab)-IgG/IgM, 58 were positive for aCL-IgG/IgM, 73 were positive for LA, 105 were positive for both β2GPⅠ Ab-IgG/IgM and aCL-IgG/IgM, 17 were positive for both β2GPⅠ Ab-IgG/IgM and LA, 2 were positive for both aCL-IgG/IgM and LA, and 3 were positive for all three antibodies. **Conclusion** Our study did not find a difference in humoral immunity between RSA women of advanced maternal age and those of low maternal age.

【**Key words**】 Advanced maternal-age Recurrent spontaneous abortion Humoral immunity

随着女性年龄增加，妊娠并发症及产科各种不良妊娠结局风险增高，其中复发性流产(recurrent spontaneous abortion, RSA)对不仅造成女性出血、感染等生理上的损伤，增加焦虑、抑郁、创伤性应激障碍和自杀等风险，也是早产、胎儿生长受限、胎盘早剥、死产等产科并发症的前哨风险指标，并且是预测女性未来心血管疾病和静脉血栓等长期健康问题的指标之一，增加个人、医疗体系和社会的经济负担[1]。

RSA病因复杂，年龄是其独立危险因素[2]。全身自身免疫性疾病(systemic autoimmune diseases, AID) 也是RSA的重要病因之一[3]。常见的妊娠合并AID包括抗磷脂综合征(antiphospholipid syndrome, APS)、系统性红斑狼疮(systemic lupus erythematosus, SLE)、干燥综合征(Sjogren's syndrome, SS)、类风湿关节炎(rheumatoid arthritis, RA)、系统性硬化症(systemic sclerosis, SSc)、未分化结缔组织病(undifferentiated connective tissue disease, UCTD)及甲状腺自身免疫(thyroid autoimmunity, TAI)疾病等[4]。随着年龄增加，AID发生率是否增高，或自身免疫状态是否发生变化，进而增加复发性流产的风险，是一个值得探讨的问题。

本研究纳入2022年1月–2023年10月在本中心就诊的RSA患者，检测各种自身抗体判断其体液免疫状态，并按照年龄分层，比较高龄RSA患者与低龄RSA患者体液免疫的差异。

1 资料与方法

1.1 一般资料

纳入2022年1月–2023年10月在上海市第一妇婴保健院生殖免疫科就诊的女性患者为研究对象。纳入标准：①临床确诊为RSA：2次及2次以上28周内自然流产，包括生化妊娠；②年龄20 ~ 45岁。排除标准：①妊娠状态；②患有RSA其他相关疾病：如夫妻染色体异常，子宫畸形，未控制的糖尿病和高血压疾病，尚未治疗或甲状腺功能不稳定的甲状腺功能亢进/甲状腺功能减退，易栓症(高同型半胱氨酸血症、蛋白S缺乏、蛋白C缺乏、抗凝血酶Ⅲ缺乏)；③上述检查资料不全。

1.2 检测方法

患者在近2周未服用药物(如短效口服避孕药、抗凝药等)及非感染情况下，空腹采静脉血。采用化学发光分析法，iFlash-3000分析仪(深圳市亚辉龙生物科技股份有限公司)及配套试剂检测抗心磷脂抗体(anticardiolipin antibodies, aCL)IgG/IgM，抗β2糖蛋白Ⅰ抗体(anti-β2 glycoprotein Ⅰ antibodies, β2GPⅠ Ab)、抗核抗体(antinuclear antibody, ANA)，抗双链DAN(anti-double stranded DNA, dsDNA)抗体；日本希森美康公司血细胞分析仪和试剂进行狼疮抗凝物(lupus anticoagulant, LA)测定；采用蛋白免疫印迹法，自动蛋白免疫印迹仪XD248(上海迅达医疗仪器有限公司)与德国胡曼生化诊断有限责任公司的试剂进行可提取核抗原(extractable nuclear antigen, ENA)抗体测定；酶联免疫法，全自动酶联免疫分析仪HB-500E(嘉兴科瑞迪医疗器械有限公司)及上海科新生物技术股份有限公司试剂进行抗α-胞衬蛋白抗体(antibodies against alpha-fodrin, AAA)及抗单链DNA(anti single-stranded DNA, ssDAN)抗体测定；采用化学发光分析法，西门子公司CENTAUR型全自动化学发光分析仪与配套试剂进行抗甲状腺过氧化物酶抗体(thyroid peroxidase antibody, TPoAb)和抗甲状腺球蛋白抗体(thyroglobulin antibody, TgAb)检测。免疫指标异常者，间隔一月后复查，两次均异常者，按照异常值处理；一次异常，一次正常，按照正常值处理。

1.3 分组

根据患者年龄分组。20 ~ 34岁为低龄组，35 ~ 45岁为高龄组。

1.4 诊断标准

各种自身免疫疾病如APS、SLE、SS、RA、UCTD的诊断方式包括两种方式。第一种方式为入组前因各种症状由风湿科确诊；第二种方式，在入组后因体液免疫指标异常，风湿科会诊后确诊。

1.5 统计学方法

比较低龄组RSA女性和高龄组RSA女性各种自身免疫标记物差异。计量资料应用Kolmogorov-Smirnov test进行正态性检验，若符合正态分布，计量资料数据采用

$\bar{x}\pm s$表示, 两组间比较采用独立样本t检验, 分类变量采用卡方检验或Fisher精确检验。采用二分类变量logistic回归分析。多变量模型中控制了可能的混杂因素, 包括体质量指数(body mass index, BMI)、既往活产史、自然流产次数, 并计算为校正的优势比(odds ratio, OR)和95%置信区间(confidence interval, CI)。所有统计分析均使用SPSS 26.0进行, 双侧$P<0.05$为差异有统计学意义。

2　结果

最终共纳入4 009例RSA患者。低龄组2 851例, 高龄组1 158例。两组患者BMI、既往活产史、自然流产次数差异均有统计学意义(表1)。

两组患者各种自身免疫疾病如APS、SLE、SS、RA、UCTD等患病率差异无统计学意义(表2)。两组研究对象抗磷脂抗体(aCL-IgG/IgM、β2GPⅠ Ab-IgG/IgM和LA)、ANA、抗ENA抗体、AAA、抗dsDNA抗体、抗ssDAN抗体和TAI阳性率差异均无统计学意义。高龄组中LA阳性率低于低龄组, 差异有统计学意义(表3)。比较两组研究对象各种自身抗体滴度, 高龄组中aCL-IgM 和β2GPⅠ Ab-IgM滴度均高于低龄组, 差异有统计学意义, aCL-IgG、β2GPⅠ Ab-IgG、LA、ANA、dsDNA、ssDAN 和TpoAb滴度无明显差异(表4)。

表 1　研究对象基本信息

Table 1　Baseline characteristics of the participants

Index	Advanced age group (n=1 158)	Low age group (n=2 851)	P
Age/yr.	37.80±2.81	30.43±2.69	<0.01
Body mass index/(kg/m^2)*	22.48±2.82	21.95±2.91	<0.01
Times of live birth	0.36±0.57	0.10±0.31	<0.01
Times of abortion	2.72±1.13	2.52±0.87	<0.01

表 2　两组患者自身免疫疾病患病率比较

Table 2　Comparison of autoimmune diseases between the two groups

Autoimmune disease	Advanced age group/case (%)	Low age group/case (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
APS	181 (15.6)	403 (14.1)	1.13 (0.90-1.36)	1.07 (0.77-1.32)
SLE	0 (0)	3 (0.1)	/	/
SS	11 (0.9)	25 (0.9)	1.08 (0.53-2.21)	0.37 (0.81-1.73)
RA	3 (0.3)	1 (0)	7.40 (0.77-71.24)	7.45 (0.72-77.87)
UCTD	275 (23.7)	644 (22.6)	1.07 (0.91-1.25)	1.10 (0.88-1.38)

Advanced age group n=1 158, low age group n=2 851. APS: antiphospholipid syndrome; SLE: systemic lupus erythematosus; SS: Sjogren's syndrome; RA: rheumatoid arthritis; UCTD: undifferentiated connective tissue disease. The results were adjusted for BMI, the times of live births, and the times of abortions.

表 3　两组患者自身抗体阳性率比较

Table 3　Comparison of positive rates of autoantibodies between the two groups

Autoimmune marker	Advanced age group/case (%)	Low age group/case (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
aPLs	221 (19.1)	557 (19.5)	0.97 (0.82-1.16)	0.95 (0.75-1.21)
aCL-IgG	20 (1.7)	51 (1.8)	0.97 (0.57-1.63)	1.16 (0.59-2.30)
aCL-IgM	37 (3.2)	68 (2.4)	1.36 (0.89-2.08)	0.99 (0.53-1.86)
β2GPⅠ Ab-IgG	7 (0.6)	28 (1.0)	0.61 (0.27-1.14)	0.74 (0.29-1.89)
β2GPⅠ Ab-IgM	189 (16.3)	431 (15.1)	1.01 (0.91-1.32)	1.08 (0.84-1.40)
LAC	19 (1.6)	76 (2.7)	0.61 (0.37-1.01)	0.36 (0.17-0.78)*
ANA	76 (6.6)	189 (6.6)	0.99 (0.75-1.30)	1.20 (0.83-1.74)
ENA	107 (9.2)	298 (10.5)	0.87 (0.69-1.10)	1.06 (0.78-1.44)
dsDNA	23 (2.0)	58 (2.0)	0.98 (0.60-1.59)	0.93 (0.56-1.89)
ssDNA	25 (2.2)	34 (1.2)	1.83 (1.09-3.01)	1.88 (0.91-3.90)
AAA	59 (5.1)	141(4.9)	1.03 (0.76-1.41)	0.98 (0.63-1.52)
TAI	206 (17.8)	480 (16.8)	1.07 (0.89-1.28)	0.99 (0.78-1.26)
TPoAb	158 (13.6)	367 (12.9)	1.07 (0.88-1.31)	0.97 (0.74-1.29)
TgAb	127 (11.0)	294 (10.3)	0.93 (0.75-1.16)	1.01 (0.75-1.36)

aPLs: antiphospholipid antibodies; aCL: anticardiolipin antibodies; β2GPⅠ Ab: anti-β2 glycoprotein Ⅰ antibodies; LAC: lupus anticoagulant; ANA: antinuclear antibody; ENA: extractable nuclear antigen; dsDNA: anti-double stranded DNA; ssDNA: anti-single-stranded DNA; AAA: antibodies against alpha-fodrin; TpoAb: thyroid peroxidase antibody; TgAb: thyroglobulin antibody. Advanced age group, n=1 158; low age group, n=2 851. The adjusted OR results were adjusted for BMI, the times of live births, and the times of abortions. * P<0.05.

表 4 两组研究对象自身抗体滴度比较

Table 4 Comparison of autoantibody titers between the two groups

Autoimmune marker	Advanced age group (n=1 158)	Low age group (n=2 851)	P
aCL-IgG	2.63±4.64	2.59±4.59	0.86
aCL-IgM	3.44±3.23	3.13±2.86	<0.01
β2GPⅠAb-IgG	2.59±2.36	2.93±7.30	0.05
β2GPⅠAb-IgM	10.56±33.03	7.69±17.76	<0.01
LA	1.06±0.08	1.06±0.08	0.10
ANA	15.31±51.44	17.79±59.55	0.19
dsDNA	4.91±11.32	4.98±9.03	0.83
ssDAN	3.48±7.76	3.06±5.61	0.09
TPoAb	100.56±256.18	105.88±269.44	0.55

All abbreviations are given in the footnote to Table 2.

两组患者抗磷脂抗体(antiphospholipid antibodies, aPLs)谱中三种抗体累计阳性778例, β2GPⅠAb-IgG/IgM阳性者520例, aCL-IgG/IgM阳性者58例, LA阳性者73例, β2GPⅠAb-IgG/IgM与aCL-IgG/IgM同时阳性者105例, β2GPⅠAb-IgG/IgM与LA同时阳性者17例, aCL-IgG/IgM与LA同时阳性者2例, 三种抗体均阳性者3例(图1)。

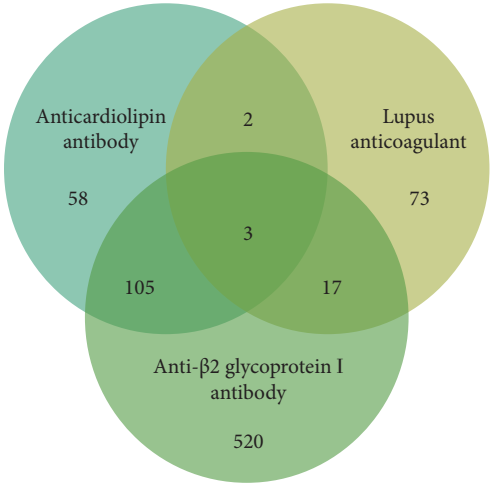

图 1 研究对象抗磷脂抗体阳性情况

Fig 1 The positive rate of antiphospholipid antibodies of patients

The numbers in the figure are the numbers of positive cases.

3 讨论

自然流产是指一定妊娠孕周前的妊娠过程失败, 主要包括生化妊娠、空孕囊、胚胎发育逐渐停止、胚胎或胎儿死亡、胚胎及其附属物排出等表现。目前我国将妊娠不足28周、胎儿体重不足1 000 g而妊娠终止者定义为自然流产[5]。欧洲人类生殖与胚胎学学会(European Society of Human Reproduction and Embryology, ESHRE)定义自然流产为妊娠24周前的妊娠丢失[2]。生化妊娠是否纳入自然流产管理尚未达成共识, 在ESHRE指南中自然流产包括了生化妊娠, 而美国生殖医学学会(American Society for Reproductive Medicine, ASRM)指南中自然流产不包括生化妊娠[6]。按照我国复发性流产诊治专家共识, 生化妊娠也是妊娠失败的一种表现形式, 属于妊娠丢失的范畴, 应纳入自然流产进行管理[7], 因此本研究中将生化妊娠纳入自然流产结局中。

女性35岁后卵子质量下降、胚胎非整倍体率增高及生育能力下降[8]。随着女性年龄增加, 自然流产风险增高, 20 ~ 29岁自然流产风险最低, 约为12%, 40 ~ 44岁时自然流产风险为51%, 45岁后为93%[9]。胚胎染色体异常是高龄女性自然流产的重要原因, 胚胎移植前基因筛查(preimplantation genetic screening, PGS)似乎可避免孕早期流产, 然而11 项RCT研究显示PGS并没有增加高龄女性的妊娠成功率, 甚至降低了活产率[10]。另有研究发现PGS可以增加活产率, 但未发现对自然流产的影响[11]。因此高龄导致的自然流产可能存在其他病因, 如代谢异常、子宫环境异常、自身免疫异常等。而自身免疫性疾病不仅好发于女性, 并且与各种不良妊娠结局风险增高有关[12]。

在妊娠状态下, 母体产生的自身抗体和(或)自身反应性淋巴细胞以及某些细胞因子可攻击滋养层细胞、母-胎界面血管内皮细胞及胎儿细胞, 影响胚胎的种植及随后的生长发育, 严重者可导致RSA, 与此同时, 妊娠期雌激素水平上升可激活体液免疫途径, 使原有自身免疫疾病的活动度上升, 病情进展严重者可危及母婴生命[13]。大约20%的RSA女性存在自身免疫状态异常, 如aPLs、ANA、TPoAb、TgAb等自身抗体异常[14]。本研究尚未发现高龄组与低龄组各种自身免疫疾病存在差异。

3.1 抗磷脂抗体与高龄RSA的关系

aPLs是一组以磷脂和/或磷脂结合蛋白为靶抗原的自身抗体总称。aPLs主要存在于APS等自身免疫病患者中, 是APS最具特征的实验室指标, 在RSA人群中APS发病率为5% ~ 20%[15]。本研究中高龄和低龄RSA女性aPLs阳性率分别为19.1%和19.5%, 与既往研究报道基本一致。aPLs低滴度阳性可见于健康人群以及传染性疾病、药物、恶性肿瘤等[16]。有研究发现, 即使未诊断APS, aPL阳性的女性比aPL阴性的女性流产率更高(RR= 1.68, 95%CI:1.24 ~ 2.28)[17]。一项基于德国人群的前瞻性研究发现aCL-IgM和β2GPⅠ-IgM滴度随着年龄增加而增加, 而aCL-IgG和β2GPⅠ-IgG与年龄关系不大[18]。本研究尽管未发现高龄组和低龄组中aCL-IgG/M和β2GPⅠ-IgG/M阳性率有差异, 但比较两组抗体滴度发现, 高龄组中aCL-

IgM和β2GPⅠ-IgGM滴度高于低龄组, 差异有统计学意义, 与上述研究报道一致。高龄组中LA阳性率低于低龄组, 与LA阳性人群普遍年轻化有关。同时本研究发现在aPLs谱中β2GPI-IgG/IgM占比较高, LA次之, 而aCL-IgG/IgM占比最少。

3.2　抗核抗体与高龄RSA的关系

ANA是筛查和诊断各种风湿性疾病重要的实验室指标, ANA的存在与各种自身免疫疾病有关, 包括SLE、SSc、SS、混合性结缔组织病(mixed connective tissue disease, MCTD)和特发性炎性肌病[19]。ANA导致自然流产的可能机制包括对卵母细胞和胚胎发育产生直接不利影响、免疫复合物在母胎界面沉积及免疫复合物诱导局部补体激活和炎症浸润[20]。

2020年一项Meta分析发现, RSA患者ANA 阳性率明显高于对照组(OR= 2.97, 95%CI: 1.91 ~ 4.64), ANA阳性和不明原因RSA之间存在明显关联(OR= 3.27, 95%CI: 2.01 ~ 5.31), 即使尚未诊断自身免疫性疾病的女性, ANA阳性也与RSA风险增加显著相关(OR= 2.23, 95%CI: 1.40 ~ 3.55)[21]。即使采用辅助生殖技术受孕, ANA阳性女性的自然流产率增加(OR= 3.25, 95%CI: 1.57 ~ 6.76), 移植成功率降低(OR= 0.51, 95%CI: 0.36 ~ 0.72)[22]。有研究提示, 随着年龄增高, ANA在健康人群中的阳性率增高[23]。本研究发现两组研究对象ANA阳性率均为6.6%, 未发现差异有统计学意义, 可能与本研究纳入人群为生育期女性, 总体年龄偏低有关。

3.3　其他抗体与高龄RSA的关系

ENA抗体包括一系列针对细胞核中抗原成分的自身抗体, 包括抗Sm抗体、抗Ro/SSA抗体、抗SSB抗体、抗Jo-1抗体、抗U1-RNP抗体和抗r-RNP抗体等, 这些抗体存在于各种风湿病的分类标准中[19]。ENA抗体对于诊断结缔组织病, 如SLE、MCTD、SS、多肌炎和皮肌炎等有较高的临床诊断价值, 而这些自身免疫疾病与复发性流产相关。抗SSA抗体和抗SSB抗体是SLE和SS患者中常见的抗体[24]。2023年一项Meta分析提示SLE女性(OR= 4.90, 95%CI: 3.10 ~ 7.69)和SS女性(RR= 8.85, 95%CI: 3.10 ~ 25.26)自然流产风险增加[12]。抗SSA和/或抗SSB还可能与类风湿性关节炎相关[25]。抗SSA/SSB阳性, 但未达到自身免疫疾病的诊断标准女性中, 外周血中各种免疫细胞及细胞因子紊乱, 采用辅助生殖技术助孕者后临床妊娠率、着床率均显著较低[26], 并增加各种不良妊娠结局[27]。本研究发现高龄与低龄组间ENA抗体差异无统计学意义。

抗dsDNA抗体对SLE的诊断及分类具有高度特异性[28]。联合抗体检测可以有效提高SLE的检出率[29]。AAA抗体对干燥综合征的诊断有一定的意义[30]。本研究发现高龄组与低龄组抗dsDNA抗体、抗ss-DNA抗体和AAA抗体差异均无明显统计学意义。

甲状腺自身免疫(thyroid autoimmunity, TAI)是指体内存在TPoAb和/或TGAb阳性[31]。约17% ~ 33%的RSA女性存在TPoAb或TgAb阳性[32]。2023年一项Meta分析提示TAI增加自然流产风险(OR= 2.77, 95%CI: 2.10 ~ 3.65)[12], TAI女性RSA率高于非TAI女性[33]。本研究发现低龄组RSA女性中TAI发生率16.8%, 高龄组RSA女性中17.8%, 两组比较未发现差异有统计学意义。

4　结论

本研究主要探讨高龄RSA女性中体液免疫状态是否与低龄RSA女性存在差异, 研究发现高龄组和低龄组APS、SLE、SS、RA、UCTD无明显差异。高龄组中aCL-IgM和β2GPⅠ-IgGM滴度高于低龄组, 但两组阳性率无明显差异, 高龄RSA女性中LA阳性率高于低龄组, 差异有统计学意义, 其他自身抗体阳性率差异无统计学意义。因此本研究尚未发现高龄RSA女性与低龄RSA女性体液免疫差异。

本研究有许多不足之处, 首先, RSA女性中各种自身抗体指标异常并不能确诊为特定的自身免疫疾病, 如ANA是一种高敏感但非特异性的标记物, 其在健康人群中具有一定的阳性率; 其次本研究为单中心研究, 由于不同的体液免疫标记物检测方法学之间存在假阳性或假阴性, 因此本中心数据与其他中心不具有可比性, 仅代表本中心数据。

*　　*　　*

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