

doi: 10.3978/j.issn.2095-6959.2021.03.012

View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2021.03.012>

妊娠期甲状腺功能减退对母婴妊娠结局的影响

赵一芳, 顾颖

(无锡市妇幼保健院产科, 江苏 无锡 214001)

[摘要] 目的: 探讨妊娠期甲状腺功能减退(以下简称甲减)对母婴妊娠结局的影响。方法: 选取2016年1月至2019年6月在无锡市妇幼保健院产科门诊检查并住院分娩的甲减孕妇771例, 其中临床甲减病例81例作为甲减组、临床亚甲减病例690例作为亚甲减组, 随机选取同期420例正常孕妇为对照组, 对其甲状腺功能(TSH和FT4水平)、妊娠并发症及结局(妊娠期糖尿病、妊娠期高血压疾病、胎膜早破、羊水异常、产后出血)、围产儿不良结局(胎儿宫内窘迫、流产或死胎、早产、新生儿窒息等)进行比较分析。结果: 30 698例孕妇中甲减发生率为2.51% (771/30 698)。3组间年龄、孕前BMI、产次和孕周的比较, 差异无统计学意义($P < 0.05$)。甲减组、亚甲减组在孕中期、孕晚期的TSH水平均高于对照组($P < 0.05$), FT4水平均低于对照组($P < 0.05$); 甲减组在孕中期、孕晚期的TSH水平高于亚甲减组($P < 0.05$), FT4水平低于亚甲减组($P < 0.05$)。甲减组的妊娠糖尿病、妊娠期高血压疾病、胎膜早破、羊水异常等的发生率均高于对照组($P < 0.05$), 亚甲减组的妊娠糖尿病、妊娠期高血压疾病、胎膜早破等发生率高于对照组($P < 0.05$), 而甲减组的妊娠糖尿病、胎膜早破等发生率水平高于亚甲减组($P < 0.05$)。甲减组、亚甲减组的胎儿宫内窘迫、早产及新生儿窒息发生率均高于对照组($P < 0.05$), 而甲减组的新生儿窒息发生率高于对照组($P < 0.05$)。结论: 孕妇有较高的甲减发生率, 并与母婴不良结局增加有关; 应早期筛查和治疗妊娠期甲减, 控制孕妇甲状腺激素水平, 改善母婴妊娠结局。

[关键词] 甲状腺功能减退; 妊娠期; 妊娠结局; 妊娠并发症

Effect of hypothyroidism during pregnancy on maternal and infant pregnancy outcomes

ZHAO Yifang, GU Ying

(Department of Obstetrics, Wuxi Maternal and Child Health-Care Hospital, Wuxi Jiangsu 214001, China)

Abstract **Objective:** To explore the effect of hypothyroidism during pregnancy on maternal and infant pregnancy outcomes. **Methods:** A total of 771 cases of hypothyroid pregnant women who were examined in the obstetric outpatient department and hospitalized for delivery in Wuxi Maternity and Child Health Hospital from January 2016 to June 2019 were selected as subjects. Among them, 81 cases of clinical hypothyroidism were regarded as hypothyroidism

收稿日期 (Date of reception): 2020-11-21

通信作者 (Corresponding author): 赵一芳, Email: zhaoyifang126@126.com

基金项目 (Foundation item): 江苏省妇幼健康科研项目 (F201735); 无锡市科技发展资金项目 (CSE31N1718)。This work was supported by Jiangsu Provincial Maternal and Child Health Research Project (F201735) and Wuxi Science and Technology Development Fund Project (CSE31N1718), China.

group, and 690 cases of clinical hypothyroidism cases were regarded as hypomethylene group, and randomly sampling 420 cases of normal pregnant women as control group. Then comparative analysis on thyroid function (TSH and FT4 levels), pregnancy complications and outcomes (gestational diabetes, gestational hypertension, premature rupture of membranes, abnormal amniotic fluid, postpartum hemorrhage), adverse perinatal outcomes (fetal distress, miscarriage or stillbirth, premature birth, neonatal asphyxia, etc.) were adopted. **Results:** The incidence rate of hypothyroidism in the 30 698 cases of pregnant women was 2.51% (771/30 698). There was no significant difference in age, BMI before pregnancy, parity and gestational week among the three groups ($P<0.05$). TSH levels in the second and third trimesters of hypothyroidism and hypomethylene were higher than those of the control group ($P<0.05$), and FT4 levels were lower than those of the control group ($P<0.05$); the level of TSH in the second and third trimesters of the hypothyroidism group was higher than that of the hypothylyene group ($P<0.05$), and the level of FT4 was lower than that of the hypothylyene group ($P<0.05$). The incidences of gestational diabetes, gestational hypertension, premature rupture of membranes, and abnormal amniotic fluid in the hypothyroid group were higher than those in the control group ($P<0.05$). In the hypothylyene group, the incidence of gestational diabetes, gestational hypertension, and premature rupture of membranes was higher than that of the control group ($P<0.05$), while the incidence of gestational diabetes and premature rupture of membranes in the hypothylyene group was higher than that of the hypothyroid group ($P<0.05$). The incidences of fetal distress, premature delivery and neonatal asphyxia in the hypothyroid group and hypothylyene group were higher than those in the control group ($P<0.05$), while the incidence of neonatal asphyxia in the hypothyroidism group was higher than that in the control group ($P<0.05$). **Conclusion:** Pregnant women have a relatively high incidence rate of hypothyroidism during pregnancy. We should early screen and treat hypothyroidism during pregnancy, adjust thyroid hormone level in pregnant women, to improve pregnancy outcomes of maternal and infant.

Keywords hypothyroidism; pregnancy; pregnancy outcome; pregnancy complication

甲状腺功能减退(以下简称甲减)是孕妇较为常见的并发症,包括临床甲减和亚甲减,其发生率为2%~5%^[1];而亚甲减是孕妇最为常见的类型,所占比重较大,表现为血清游离甲状腺激素正常,而促甲状腺激素升高^[2]。研究^[3]显示:在390例未进行治疗的亚甲减患者中,有45%发展为甲减,30%表现为无症状的亚临床征象,约15%恢复至正常水平。由此可见,对孕妇进行早期诊断和治疗显得尤为必要。本研究对无锡市妇幼保健就诊的771例甲减(包括临床甲减和亚甲减)病例进行随访,并以420例正常孕妇为对照,探讨不同类型甲减病例的甲状腺激素水平及其与母婴妊娠结局的关系,现报告如下。

1 对象与方法

1.1 对象

选取2016年1月至2019年6月在无锡市妇幼保健院产科检查并分娩的30 698例初产或1次顺产史的经产孕妇进行甲状腺筛查,其中筛查出81例临床甲减病例作为甲减组,690例临床亚甲减病例作为

亚甲减组。甲减诊断标准^[4]:临床甲减为游离四碘甲腺原氨酸(FT4)水平下降($<12\text{ pmol/L}$),而促甲状腺激素(thyroid stimulating hormone, TSH)水平升高($>4.0\text{ mU/L}$);临床亚甲减表现为FT4水平正常($12\sim22\text{ pmol/L}$),而TSH水平升高($>4.0\text{ mU/L}$)。甲减发生率为2.51% (771/30 698);同时随机选取420例正常孕妇作为对照组。

1.2 方法

治疗方法:甲减的孕妇从诊断明确起,给予左甲状腺素钠片(雷替斯,德国Berlin-Chemie AG公司, H20110178, $50\text{ }\mu\text{g}\times100$ 片)口服, TSH在 $2.5\sim5.0\text{ mU/L}$ 、 $5.0\sim8.0\text{ mU/L}$ 、 $>8.0\text{ mU/L}$ 时,雷替斯的开始剂量分别为 $50\text{ }\mu\text{g/d}$ 、 $75\text{ }\mu\text{g/d}$ 、 $100\text{ }\mu\text{g/d}$,每半个月检测1次血清TSH和FT4,根据检测结果酌情调整药量,待TSH $<2.5\text{ mU/L}$ 后药量恒定,继续口服,每月检测1次,直至妊娠结束。

1.3 观察指标

1)甲状腺功能评估:抽取各组孕妇空腹静脉血5 mL,采用放射免疫疗法检测孕中期、孕晚期

游离血清中的TSH和FT4水平。2)妊娠并发症及妊娠结局:观察各组孕妇孕期的并发症和妊娠结局,进行OGTT筛查、血压监测,观察各组妊娠糖尿病、妊娠期高血压疾病、胎膜早破、羊水异常、产后出血的发生情况。3)围产儿结局:进行B超监测胎儿宫内状况、孕晚期胎儿电子胎心监护、新生儿Apgar评分,观察胎儿宫内窘迫、流产或死胎、早产、新生儿窒息等的发生情况。

1.4 统计学处理

采用SPSS 21.0统计学软件对数据进行分析。计量资料以均数 $\pm$ 标准差($\bar{x}\pm s$)表示,多组间比较采用单因素方差分析,组间两两比较采用SNK-q检验;计数资料以例(%)表示,组间比较则采用卡方(χ^2)检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 一般资料

3组的年龄、孕前体重指数(body mass index, BMI)、产次、孕周等资料比较,差异均无统计学

意义(均 $P>0.05$,表1)。

2.2 3组孕中期、晚期TSH和FT4水平比较

甲减组、亚甲减组在孕中期、孕晚期的TSH水平均高于对照组($P<0.05$),FT4水平均低于对照组($P<0.05$);甲减组在孕中期、孕晚期的TSH水平高于亚甲减组($P<0.05$),FT4水平低于亚甲减组($P<0.05$,表2)。

2.3 3组妊娠并发症及妊娠结局比较

甲减组的妊娠糖尿病、妊娠期高血压疾病、胎膜早破、羊水异常的发生率均高于对照组($P<0.05$),亚甲减组的妊娠糖尿病、妊娠期高血压疾病、胎膜早破等发生率也高于对照组($P<0.05$),而甲减组的妊娠糖尿病、胎膜早破等发生率水平又高于亚甲减组($P<0.05$,表3)。

2.4 3组围产儿结局比较

甲减组、亚甲减组的胎儿宫内窘迫、早产及新生儿窒息发生率均高于对照组($P<0.05$),而甲减组的新生儿窒息发生率高于亚甲减组($P<0.05$,表4)。

表1 3组孕产妇的一般资料比较

Table 1 Comparison on general data in 3 groups of pregnant women

组别	<i>n</i>	年龄/岁	孕前BMI/(kg·m ⁻²)	产次(初产/经产)	孕周
对照组	420	26.27 $\pm$ 3.45	21.59 $\pm$ 1.70	331/89	37.90 $\pm$ 2.75
亚甲减组	690	26.19 $\pm$ 3.51	21.83 $\pm$ 1.85	563/127	37.59 $\pm$ 3.35
甲减组	81	26.43 $\pm$ 3.28	21.94 $\pm$ 1.92	62/19	37.48 $\pm$ 2.89
<i>F</i> / χ^2		0.202	2.730	2.040	1.467
<i>P</i>		0.817	0.066	0.361	0.231

表2 3组孕产妇的TSH和FT4比较

Table 2 Comparison on TSH and FT4 in 3 groups of pregnant women

组别	<i>n</i>	孕中期		孕晚期	
		TSH/(mU·L ⁻¹)	FT4/(pmol·L ⁻¹)	TSH/(mU·L ⁻¹)	FT4/(pmol·L ⁻¹)
对照组	420	1.39 $\pm$ 0.47	15.74 $\pm$ 3.61	0.96 $\pm$ 0.45	14.71 $\pm$ 3.07
亚甲减组	690	3.84 $\pm$ 0.82*	13.58 $\pm$ 3.24*	1.57 $\pm$ 0.66*	13.90 $\pm$ 2.75*
甲减组	81	5.37 $\pm$ 1.05* [#]	10.42 $\pm$ 2.89* [#]	2.04 $\pm$ 0.68* [#]	11.83 $\pm$ 2.67* [#]
<i>F</i>		1573.352	106.026	188.230	36.257
<i>P</i>		<0.001	<0.001	<0.001	<0.001

与对照组比较,* $P<0.05$;与亚甲减组比较,[#] $P<0.05$ 。

Compared with the control group,* $P<0.05$; compared with the hypothyroidism group,[#] $P<0.05$.

表3 3组孕产妇妊娠并发症及其妊娠结局比较分析结果

Table 3 Comparison on pregnancy complications and outcomes in 3 groups of pregnant women

组别	n	妊娠糖尿病/[例(%)]	妊娠期高血压疾病/[例(%)]	胎膜早破/[例(%)]	羊水异常/[例(%)]	产后出血/[例(%)]
对照组	420	10 (2.38)	24 (5.71)	11 (2.62)	22 (5.24)	9 (2.14)
亚甲减组	690	51 (7.39)*	70 (10.14)*	55 (7.97)*	58 (8.41)	16 (2.38)
甲减组	81	12 (14.81)* [#]	13 (16.05)*	21 (25.93)* [#]	11 (13.58)*	3 (3.70)
χ^2		22.786	11.574	55.551	8.057	0.728
P		<0.001	0.003	<0.001	0.018	0.695

与对照组比较, *P<0.05; 与亚甲减比较, [#]P<0.05。

Compared with the control group, *P<0.05; compared with the hypothyroidism group, [#]P<0.05.

表4 3组孕产妇的围产儿结局比较

Table 4 Comparison on perinatal outcomes in 3 groups of pregnant women

组别	n	胎儿宫内窘迫/[例(%)]	流产或死胎/[例(%)]	早产/[例(%)]	新生儿窒息/[例(%)]
对照组	420	13 (3.10)	3 (0.71)	8 (1.90)	15 (3.57)
亚甲减组	690	42 (6.09)*	14 (2.02)	45 (6.52)*	48 (6.96)*
甲减组H	81	8 (9.88)*	3 (3.70)	9 (11.11)*	13 (16.05)* [#]
χ^2		8.314	4.891	17.420	18.607
P		0.016	0.087	<0.001	<0.001

与对照组比较, *P<0.05; 与亚甲减比较, [#]P<0.05。

Compared with the control group, *P<0.05; compared with the hypothyroidism group, [#]P<0.05.

3 讨论

妊娠期甲减影响孕妇甲状腺功能水平。女性在妊娠期会分泌多种胎盘激素, 这可能会影响下丘脑-垂体-甲状腺轴, 从而影响孕妇的甲状腺功能; 在妊娠期间母体和胎儿对甲状腺素的需求量也会明显增加, 再加上孕妇的肾小球过滤率会升高, 使得碘流失增加^[5]。此外, 妊娠期间随着雌激素分泌增多, 刺激甲状腺结合蛋白的分泌, 从而导致孕妇甲状腺功能下降^[6]。本研究结果显示: 约有90%妊娠期甲减病例为亚甲减患者, 多数无明显的症状体征, 在临床上容易漏诊, 错过了最佳纠正甲状腺功能的时机。甲状腺激素在人体生长发育、组织细胞分化、物质能量代谢等过程中有重要的意义, 尤其是对胎儿的大脑组织和神经发育至关重要^[7]。妊娠期甲减对母体的免疫系统、内分泌系统等也有诸多不良影响, 引起妊娠期并发症和不良妊娠结局。本研究结果显示: 妊娠期甲减容易产生各种妊娠并发症, 如妊娠糖尿病、妊娠期高血压疾病、胎膜早破、羊水异常等。何颖等^[8]

也证实妊娠合并甲减对母体影响较大。妊娠期甲减会导致孕妇记忆力减退、反应迟钝、嗜睡、肌无力等, 严重者会出现心力衰竭, 对血糖、血脂等也产生影响。甲状腺激素具有增强肝糖异生, 促进胰高血糖素、肾上腺素、生长激素、皮质醇等的生糖作用, 使得孕妇血糖升高, 引起妊娠期糖尿病^[9]。而引起妊娠高血压疾病原因是抗甲状腺抗体在孕妇血管内逐渐形成免疫复合物并沉积, 使得外周血管阻力增加, 继发交感神经张力和肾上腺素能的相关应答反应^[10]。本研究结果显示: 妊娠期甲减对围产儿结局产生不良影响, 表现为胎儿宫内窘迫、早产、新生儿窒息等, 这与侯美芹等^[11]报道的结果相近。甲状腺激素主导蛋白质合成和能量代谢, 妊娠期甲状腺激素缺乏会引起神经系统、脑组织发育不良, 表现为发育迟缓、身材矮小、智力低下等, 增加流产、早产、胎儿宫内窘迫、新生儿窒息等并发症概率^[12]。由此可见, 应在孕早期(妊娠12周内)加强甲状腺功能筛查, 对于甲减患者应尽早给予雷替斯等激素进行替代疗法, 并定期复查患者的甲状腺激素水平,

将甲状腺激素水平控制在合理范围内, 对改善母婴妊娠并发症和结局具有重要意义。

参考文献

1. 宋春红. 妊娠合并甲状腺功能减退和亚临床甲状腺功能减退筛查的临床意义[J]. 中华全科医师杂志, 2015, 14(8): 620-622.
SONG Chunhong. The clinical significance of screening for pregnancy with hypothyroidism and subclinical hypothyroidism[J]. Chinese Journal of General Practitioners, 2015, 14(8): 620-622.
2. 中华医学会内分泌学分会. 妊娠和产后甲状腺疾病诊治指南(2版)[J]. 中华内分泌代谢杂志, 2019, 35(8): 636-665.
Endocrinology Branch of Chinese Medical Association. Guidelines for the diagnosis and treatment of thyroid diseases in pregnancy and postpartum (second edition)[J]. Chinese Journal of Endocrinology and Metabolism, 2019, 35(8): 636-665.
3. 方碧梅. 亚临床甲状腺功能减退与妊娠期糖尿病的关系[J]. 重庆医学, 2014, 43(34): 4684-4685.
FANG Bimei. The relationship between subclinical thyroid function decline and gestational diabetes[J]. Chongqing Medical Journal, 2014, 43(34): 4684-4685.
4. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum[J]. Official Journal of the American Thyroid Association, 2017, 27(3): 315-389.
5. 李玉芳, 郑艳, 范群, 等. 妊娠期合并甲状腺功能减退的筛查及转归[J]. 海南医学, 2016, 27(24): 4033-4035.
LI Yufang, ZHENG Yan, FAN Qun, et al. Screening and outcome of hypothyroidism during pregnancy[J]. Hainan Medicine, 2016, 27(24): 4033-4035.
6. 刘志红. 妊娠合并甲状腺功能减退对妊娠结局的影响[J]. 中国妇幼保健, 2016, 31(5): 918-920.
LIU Zhihong. The influence of pregnancy with hypothyroidism on pregnancy outcome[J]. China Maternal and Child Health Care, 2016, 31(5): 918-920.
7. 孙萍, 宋佳卉, 张文莉, 等. 妊娠早期亚临床甲状腺功能减退的干预对妊娠结局的影响[J]. 宁夏医科大学学报, 2017, 39(7): 814-816.
SUN Ping, SONG Jiahui, ZHANG Wenli, et al. The effect of intervention of subclinical hypothyroidism in early pregnancy on pregnancy outcome[J]. Journal of Ningxia Medical University, 2017, 39(7): 814-816.
8. 何颖, 王海鹰, 王海文. 妊娠合并甲状腺功能减退的临床诊断及转归效果观察[J]. 中国妇幼保健, 2017, 32(14): 3135-3136.
HE Ying, WANG Haiying, WANG Haiwen. Clinical diagnosis and outcome observation of pregnancy complicated with hypothyroidism[J]. China Maternal and Child Health Care, 2017, 32(14): 3135-3136.
9. 赵叶芳, 王炳杰, 焦亚楼, 等. 亚临床甲状腺功能减退合并妊娠期糖尿病对妊娠结局的影响[J]. 现代预防医学, 2016, 43(3): 443-445, 459.
ZHAO Yefang, WANG Bingjie, JIAO Yalou, et al. The influence of subclinical hypothyroidism combined with gestational diabetes on pregnancy outcome[J]. Modern Preventive Medicine, 2016, 43(3): 443-445, 459.
10. Kim HS, Kim BJ, Oh S, et al. Gestational age - specific cutoff values are needed for diagnosis of subclinical hypothyroidism in early pregnancy[J]. J Korean Med Sci, 2015, 30(9): 1308-1312.
11. 侯美芹, 王治洁, 侯克柱. 妊娠期妇女甲状腺功能减退对妊娠结局和胎儿影响的分析[J]. 中华流行病学杂志, 2016, 37(5): 722-724.
HOU Meiqin, WANG Zhijie, HOU Kezhu. Analysis of the influence of hypothyroidism in pregnant women on pregnancy outcome and fetus[J]. Chinese Journal of Epidemiology, 2016, 37(5): 722-724.
12. 柴丽娅, 刘立立, 佟玉, 等. 左旋甲状腺素片治疗孕早期合并亚临床甲状腺功能减退对妊娠结局的影响[J]. 中国妇幼保健, 2018, 33(21): 4866-4869.
CHAI Liya, LIU Lili, TONG Yu, et al. Effect of levothyroxine tablets in the treatment of early pregnancy with subclinical hypothyroidism on pregnancy outcome[J]. China Maternal and Child Health Care, 2018, 33(21): 4866-4869.

本文引用: 赵一芳, 顾颖. 妊娠期甲状腺功能减退对母婴妊娠结局的影响[J]. 临床与病理杂志, 2021, 41(3): 566-570. doi: 10.3978/j.issn.2095-6959.2021.03.012

Cite this article as: ZHAO Yifang, GU Ying. Effect of hypothyroidism during pregnancy on maternal and infant pregnancy outcomes[J]. Journal of Clinical and Pathological Research, 2021, 41(3): 566-570. doi: 10.3978/j.issn.2095-6959.2021.03.012