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妊娠期妇女甲状腺功能的筛查情况及相关影响因素分析*

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摘要 目的: 了解妊娠期妇女甲状腺功能的筛查情况及相关影响因素。方法: 以 2016 年 1 月~2017 年 1 月在我院接受产前检查的 400 例孕妇为研究对象, 其中早期妊娠 78 例、中期妊娠 146 例、晚期妊娠 176 例, 同期健康体检合格妇女 120 例为对照组。比较妊娠期妇女和对照组促甲状腺激素(TSH)、游离 T3(FT3)及游离 T4(FT4)水平, 并分析妊娠合并甲状腺功能异常者妊娠不良结局发生情况, 并分析妊娠合并甲状腺功能异常的影响因素。结果: 400 例孕妇中, 亚临床甲减 62 例、临床甲减 5 例、亚临床甲亢 16 例、临床甲亢 2 例, 甲状腺疾病合计 85 例。孕早期 TSH 低于孕中期及孕晚期, FT3 浓度高于孕中期及孕晚期, FT4 浓度高于孕中期及孕晚期, 孕中期及孕晚期 TSH 水平高于对照组, 孕中期及孕晚期 FT3、FT4 浓度低于对照组, 差异有统计学意义($P<0.05$)。不同年龄、流产次数、碘摄入量、吸烟组妊娠合并甲状腺功能异常率差异比较有统计学意义($P<0.05$)。Logistic 回归分析, 年龄 ≥ 30 岁、流产次数 ≥ 2 次、碘摄入量 $\geq 150 \mu\text{g}/\text{d}$ 为妊娠合并甲状腺功能异常发生的独立危险因素。妊娠合并甲状腺功能异常组妊娠不良结局合计率高于妊娠合并甲状腺功能正常组($P<0.05$)。结论: 加强对妊娠期妇女甲状腺功能的筛查和高危因素的管理能够预防不良妊娠结局, 达到优生优育。

关键词: 妊娠妇女; 甲状腺功能筛查; 影响因素

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Analysis of Thyroid Function Screening in Pregnant Women and Related Influencing Factors*

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ABSTRACT Objective: To analyze the screening situation of thyroid function in pregnant women and related influencing factors.

Methods: 400 pregnant women who underwent prenatal examination in our hospital's maternity clinic from January 2016 to January 2017 were selected as the research objects, including 78 cases of early pregnancy, 146 cases of mid-term pregnancy and 176 cases of late pregnancy, and 120 pregnant women who underwent health examination in our hospital's outpatient clinic during the same period were selected as the control group. The incidence of thyroid dysfunction in pregnant women was analyzed. The levels of thyroid stimulating hormone (TSH), free T3(FT3) and free T4(FT4) were compared between pregnant women and control group. The incidence of adverse pregnancy outcomes in pregnant women with thyroid dysfunction was analyzed, the incidence of adverse pregnancy outcomes in pregnant women with thyroid dysfunction was analyzed. **Results:** Of 400 pregnant women, 62 had subclinical hypothyroidism, 5 had clinical hypothyroidism, 16 had subclinical hyperthyroidism, 2 had clinical hyperthyroidism, and 85 had thyroid diseases. TSH in the first trimester of pregnancy was lower than that in the second trimester and the third trimester of pregnancy, FT3 concentration was higher than that in the second trimester and the third trimester of pregnancy, FT4 concentration was higher than that in the second trimester and the third trimester of pregnancy, TSH level in the second trimester and the third trimester of pregnancy was higher than that in the control group, FT3 and FT4 concentration in the second trimester and the third trimester of pregnancy was lower than that in the control group, there was a statistical difference ($P<0.05$). There were statistically significant differences among different ages, abortion times, iodine intake and pregnancy complicated with thyroid dysfunction rate in smoking group ($P<0.05$). Logistic regression analysis showed that Age ≥ 30 years old, number of abortions ≥ 2 , iodine intake $\geq 150 \mu\text{g}/\text{d}$ were independent risk factors for thyroid dysfunction in pregnancy. The total rate of adverse pregnancy outcomes in pregnancy combined with thyroid dysfunction group was higher than that in pregnancy combined with normal thyroid function group ($P<0.05$). **Conclusion:** Strengthening the screening of thyroid function of pregnant women and the management of high-risk factors can prevent adverse pregnancy outcomes and achieve good prenatal and postnatal care.

Key words: Pregnant Women; Thyroid function screening; Influence factor

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前言

甲状腺为机体重要的内分泌器官,通过分泌一定量的甲状腺激素,调节机体性腺发育、代谢及生殖功能,为机体必须的激素之一^[1]。妊娠期妇女因母体血容量增加,其甲状腺功能可能随着孕妇自身生理状态的变化而相应改变,主要表现为随着妊娠周期的不断增加,血清促甲状腺激素(Thyroid stimulating hormone, TSH)浓度不断增加,游离 T₃(Free triiodothyronine, FT₃)及游离 T₄(Free thyroxine, FT₄)浓度逐渐下降^[2]。研究发现^[3,4],妊娠期妇女合并甲状腺功能异常时,甲状腺功能减退的发生率相对较高。目前妊娠合并甲状腺功能异常对子代脑发育及妊娠结局形成的不良影响已得到临床共识,甲状腺激素为胎儿及新生儿大脑发育的重要激素,能够诱导神经元增殖分化,参与神经胶质细胞生长及髓鞘形成,胚胎期缺乏甲状腺激素可能影响神经元的发育,导致子代脑发育产生不可逆损伤^[5,6]。另外妊娠期妇女甲状腺功能异常能够增加早产、流产风险。Costantine MM 等^[7]研究也表明,妊娠期甲状腺功能失调可能和孕妇产后抑郁、甲状腺炎有一定关系。临床资料报道^[8,9],妊娠期甲状腺功能异常经有效干预后能够明显改善母婴结局。研究发现^[10,11],妊娠期甲状腺疾病和多种高危因素有关。因此妊娠期妇女甲状腺功能的早期筛查及相关影响因素的分析对围产期母婴保健有重要作用。本研究主要旨在研究妊娠期妇女甲状腺功能筛查情况,和甲状腺功能异常的相关危险因素,为妊娠期甲状腺疾病的诊治提供相关依据。

1 资料与方法

1.1 研究对象

选择 2016 年 1 月~2017 年 1 月在我院产科门诊进行产前检查的 400 例孕妇为研究对象,入选标准^[12]:自然受孕,单胎妊娠;孕周明确;妊娠前无甲状腺疾病发生;病例资料完整。排除标准:既往接受头颈部放射治疗;服用对甲状腺激素有影响药物;甲状腺疾病个人史及家族史;已知甲状腺肿大;合并自身免疫性疾病、内分泌疾病;妊娠并发症;妊娠剧吐。400 例孕妇中早期妊娠 78 例(妊娠 1~12 周),年龄(22~38)岁,平均(28.05±3.11)岁;中期妊娠 146 例(妊娠 13~27 周),年龄(21~37)岁,平均(28.41±3.75)岁;晚期妊娠(妊娠 28~40 周)176 例,年龄(22~36)岁,平均(28.25±3.39)岁。收集同期我院门诊健康体检妇女 120 例为对照组,月经周期正常,无甲状腺肿大及甲状腺疾病既往史和家族史和自身免疫性病变、未服用对甲状腺功能

有影响药物,年龄(22~38)岁,平均(27.94±3.59)岁。各组年龄比较无统计学差异($P>0.05$)。

1.2 资料采集

采集妊娠期妇女的姓名、年龄、孕周、体重指数、流产次数、生育史、尿碘和吸氧情况。

1.3 实验方法

采集所有孕妇孕早期、孕中期及孕晚期和对照组空腹外周静脉血 2 mL,常规离心 5 min,保留血清。用全自动放射性免疫化学发光法测定 TSH、FT₃、FT₄ 水平。临床推荐妊娠早期、中期和晚期 TSH 分别为 0.02~4.07 mIU/L、0.09~4.10 mIU/L、0.58~5.32 mIU/L。FT₃ 分别为 0.62~5.77 pmol/L、3.24~5.61 pmol/L、2.91~5.01 pmol/L。FT₄ 分别为 6.50~22.26 pmol/L、6.50~13.02 pmol/L、5.53~10.75 pmol/L。

1.4 妊娠期甲状腺疾病诊断标准

(1)亚临床甲状腺功能减退(亚临床甲减):妊娠早期 TSH 浓度范围在 2.5~10.0 mIU/L,妊娠中晚期 TSH 范围在 3~10 mIU/L、FT₄ 水平正常。(2)临床甲状腺功能减退(临床甲减):TSH 浓度≥10.0 mIU/L,或者 TSH 浓度增加,且伴 FT₄ 水平下降。(3)亚临床甲状腺功能亢进(亚临床甲亢):排除其他因素对 TSH 的影响,TSH 较检测下限低或 TSH<0.1mIU/L,FT₄ 及 FT₃ 水平在正常范围内。(4)临床甲状腺功能亢进(临床甲亢):TSH 低于检测下限或 TSH<0.1 mIU/L,同时伴 FT₄ 浓度上升^[13]。

1.5 妊娠结局随访

所有筛查出妊娠期甲状腺功能异常妇女均进行系统、正规治疗。统计妊娠期糖尿病、妊娠期高血压疾病、贫血、自然流产、早产、低体质量儿、胎儿生长受限等不良妊娠结局^[13]。

1.6 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用($\bar{x} \pm s$)表示,选用 t 检验,计数资料用[例(%)]表示,用 χ^2 检验比较,妊娠期甲状腺功能异常的相关因素用多因素 Logistic 回归分析, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 各组 TSH、FT₃、FT₄ 水平分析

孕早期 TSH 低于孕中期及孕晚期,FT₃ 浓度高于孕中期及孕晚期,FT₄ 浓度高于孕中期及孕晚期,孕中期及孕晚期 TSH 水平高于对照组,孕中期及孕晚期 FT₃、FT₄ 浓度低于对照组,比较有统计学差异($P<0.05$),见表 1。

表 1 各组 TSH、FT₃、FT₄ 水平分析($\bar{x} \pm s$)
Table 1 Analysis of TSH, FT₃ and FT₄ levels in each group($\bar{x} \pm s$)

Groups	n	TSH(mIU/mL)	FT ₃ (pmol/L)	FT ₄ (pmol/L)
Control group	120	2.25±0.35	4.86±0.61	15.79±2.35
Early pregnancy	78	1.58±0.23*	4.71±0.68	16.04±2.71
Second trimester of pregnancy	146	2.49±0.38**	4.17±0.51**	11.21±1.49**
Late pregnancy	176	2.67±0.31**	3.96±0.43**	10.97±1.68**
F		208.230	83.455	239.949
t		<0.001	<0.001	<0.001

Note: * $P<0.05$, vs control group; ** $P<0.05$, vs early pregnancy.

2.2 400 例孕妇中甲状腺疾病患病情况

甲亢 16 例、临床甲亢 2 例,甲状腺疾病合计 85 例,见表 2。

400 例孕妇中,亚临床甲减 62 例、临床甲减 5 例、亚临床

表 2 400 例孕妇中甲状腺疾病患病情况

Table 2 Prevalence of thyroid diseases in 400 pregnant women

Pregnancy staging	n	Subclinical hypothyroidism	Clinical hypothyroidism	Subclinical hyperthyroidism	Clinical hyperthyroidism	Total
Early pregnancy	78	10(12.82)	1(1.28)	8(10.26)	0(0.00)	19(24.36)
Second trimester of pregnancy	146	24(16.44)	1(0.68)	4(2.74)	1(0.68)	30(20.55)
Late pregnancy	176	28(15.91)	3(1.70)	4(2.27)	1(0.57)	36(20.45)
Total	400	62(15.50)	5(1.25)	16(4.00)	2(0.50)	85(21.25)

2.3 妊娠合并甲状腺功能异常的单因素分析

年龄、流产次数、碘摄入量、吸烟组妊娠合并甲状腺功能异常率比

不同孕前体质质量指数、妊娠周期、文化程度、孕产史组妊娠

较有统计学差异($P<0.05$),见表 3。合并甲状腺功能异常率比较无统计学差异($P>0.05$); 不同年

表 3 妊娠合并甲状腺功能异常的单因素分析

Table 3 Analysis the single factor of pregnancy complicated with thyroid dysfunction

Factor	n	Thyroid dysfunction group(n=85)	Normal thyroid function group(n=315)	χ^2	P
Age (years)					
<25	108	8(7.41)	100(92.59)	17.451	<0.001
25~29	100	24(24.00)	76(76.00)		
≥ 30	192	53(27.60)	139(72.40)		
Pregnant precursor mass index(kg/m ²)					
<18.5	51	7(13.73)	44(86.27)	1.496	0.221
≥ 18.5	349	78(22.35)	271(77.65)		
Pregnancy cycle					
Early pregnancy	78	16(20.51)	62(79.49)	0.038	0.981
Second trimester of pregnancy	146	31(21.23)	115(78.77)		
Late pregnancy	176	38(21.59)	138(78.41)		
Education level					
Below junior high school	124	31(25.00)	93(75.00)	2.527	0.283
High school	190	34(17.89)	156(82.11)		
College degree or above	86	20(23.26)	66(76.74)		
Number of abortions					
<2	144	20(13.89)	124(86.11)	6.614	0.010
≥ 2	256	65(25.39)	191(74.61)		
Maternity history					
Initial delivery	217	50(23.04)	167(76.96)	0.691	0.406
multiparity	183	35(19.13)	148(80.87)		
Iodine intake(μg/d)					
<80	80	24(30.00)	56(70.00)	18.813	<0.001
80~150	151	15(9.93)	136(90.07)		
>150	169	46(27.22)	123(72.78)		
Smoking					
Yes	25	19(76.00)	6(24.00)	44.431	<0.001
No	375	66(17.60)	309(82.40)		

2.4 妊娠期甲状腺功能异常影响的多因素分析

以发生妊娠合并甲状腺功能异常为因变量,以年龄、流产次数、碘摄入量、吸烟为自变量进行 Logistic 回归分析,年龄 $\geq$

30 岁、流产次数 ≥ 2 次、碘摄入量 $\geq 150 \mu\text{g/d}$ 为妊娠合并甲状腺功能异常发生的独立危险因素,见表 4。

表 4 妊娠期甲状腺功能异常影响的多因素分析

Table 4 Multivariate Analysis of Influence of Thyroid Dysfunction during Pregnancy

variable	β	S.E	Wald	P	OR	95%CI
Age ≥ 30 years old	0.846	0.268	6.284	0.012	2.330	1.378~3.940
Number of abortions ≥ 2	0.593	0.280	4.849	0.028	1.809	1.045~3.132
Iodine intake $\geq 150 \mu\text{g/d}$	1.441	0.629	5.245	0.022	4.226	1.231~14.508
Smoking	0.083	1.076	0.006	0.938	1.087	0.132~8.951

2.5 妊娠合并甲状腺功能异常者妊娠不良结局发生情况分析

妊娠不良结局以妊娠期糖尿病、妊娠期高血压疾病、贫血、流产、早产、低体重儿、生长受限为主,妊娠合并甲状腺功能异

常组妊娠不良结局合计率高于妊娠合并甲状腺功能正常组 ($P<0.05$),见表 5。

表 5 妊娠合并甲状腺功能异常者妊娠不良结局发生情况分析(例,%)

Table 5 Analysis of adverse pregnancy outcomes in pregnant women with thyroid dysfunction(n, %)

Groups	n	Gestational diabetes mellitus	Hypertensive disorder complicating pregnancy	Anemia	Spontaneous abortion	Premature birth	Low body mass	Fetal growth restriction	Total
Pregnancy with thyroid dysfunction group	85	2(2.35)	4(4.71)	1(1.18)	7(8.24)	4(4.71)	2(2.35)	2(2.35)	22(25.88)
Pregnancy with normal thyroid function group	315	5(1.59)	7(2.22)	0(0.00)	3(0.95)	1(0.32)	0(0.00)	0(0.00)	16(5.08) ^a

Note: VS Pregnancy with thyroid dysfunction group ^a $P<0.05$.

3 讨论

甲状腺分泌的激素能够作用于全身各组织,调节机体新陈代谢,影响各个器官功能。甲状腺疾病是妊娠妇女的常见疾病之一,相关研究报道^[14],妊娠对甲状腺亢进的影响不大。妊娠期母体对碘的需求量增加,尿碘中碘排出量较多,碘缺乏或甲状腺功能储备有限的妇女容易发生碘水平相对不足,因此妊娠期甲状腺功能减退的发生率明显高于其他妊娠期甲状腺疾病^[15,16]。既往研究认为^[17],母体甲状腺激素无法透过胎盘,妊娠期甲状腺功能异常对后代的影响尚无明确认识。国外研究发现^[18],妊娠期甲状腺激素正常分泌是确保子代正常发育的重要因素。Koehler VF 等^[19]研究也提出,妊娠 12 周之前胎儿大脑发育的甲状腺激素全部由母体提供,从而支持胎儿大脑皮层各个功能区的生长、发育,胚胎期甲状腺激素缺乏能够减少大脑神经元体积及数量,影响神经细胞增生、迁移和突触建立,导致神经元受累,脑发育障碍。因此妊娠期甲状腺疾病和优生优育有直接关联。另外妊娠期亚甲状腺疾病容易发生习惯性流产、胎盘早剥和早产^[20]。有关研究表明^[21,22],由于孕期碘需求量增加和分娩后母体自身抑制状态的解除,部分亚临床甲减妇女容易进展为产后甲状腺炎或临床甲减,导致产后水肿、畏寒和抑郁等表现。

开展妊娠期妇女早期甲状腺功能筛查能够明显提高甲状腺功能异常的检出率,减少甲状腺疾病的误诊率及漏诊率,对于妊娠不良结局的改善及出生缺陷的减少有重要作用。但由于妊娠特殊性,临床缺乏典型表现,诊断主要依靠甲状腺激素等

实验室指标^[23]。但育龄妇女妊娠后机体代谢和激素水平可产生改变,影响甲状腺相关激素分泌,其中妊娠期雌激素的增加能够促进肝脏甲状腺素结合球蛋白的产生,影响 T_4 和 TT_3 浓度^[24]。妊娠期人绒毛膜促性腺激素的 α 亚基结构和 TSH 基本类似,从而对甲状腺有刺激作用,能够影响血清 FT_4 和 TSH 浓度^[25]。妊娠期血清甲状腺激素参考值有孕龄特异性。本研究结果显示,妊娠早期妇女血清 TSH 浓度有所降低,可能与入绒毛膜促性腺激素的快速增加,可刺激甲状腺细胞 TSH 受体,促进甲状腺激素合成,反馈性抑制 TSH 分泌。随着妊娠周期的增加, TSH 水平在妊娠中、晚期不断上升,另一方面妊娠中晚期的基础代谢率上升,能够增加甲状腺激素的消耗,加上尿碘排出增加引起甲状腺激素合成较少,降低妊娠期妇女游离甲状腺激素浓度,负反馈导致 TSH 浓度上升^[26,27]。分析本研究数据,妊娠早期妇女血清 FT_3 浓度较健康非妊娠妇女低,但无显著差异,妊娠中晚期血清 FT_3 浓度则相对较低,和 Neelaveni K 等^[28]研究结果报道相似。妊娠早期妇女血清 FT_4 浓度稍增加,中期血清 FT_4 浓度降低,晚期降低最为明显,提示妊娠中晚期妇女可能处于亚临床甲减的代偿状态。但妊娠期甲状腺功能可随着不同妊娠周期产生特异性改变,和普通人群有较大差异。本研究结果发现,妊娠期妇女亚临床甲减发生率显著高于亚临床甲亢,且不同妊娠时期亚临床甲减的发生率无显著差异。目前妊娠期甲状腺功能异常对母婴的影响已得到临床共识,本研究发现,妊娠期甲状腺功能异常组妊娠不良结局发生率较无妊娠甲状腺功能异常妇女组高,提示妊娠期合并此类疾病能够影响妊娠结局。

目前尚缺乏和妊娠甲状腺功能异常的相关影响因素的大规模报道。近年来随着二胎政策的开放,妊娠妇女的年龄有所增加。随着年龄增加机体甲状腺功能可能呈不断减退的发展趋势,并表明年龄 ≥ 30 岁孕妇更容易发生妊娠期甲状腺功能异常。本研究结果显示,年龄 ≥ 30 岁者妊娠期甲状腺功能异常率相对较高,经多因素分析发现,孕妇年龄 ≥ 30 岁是妊娠期甲状腺功能异常发生的独立影响因素,能够增加此类疾病的发生风险。研究表明,甲减可能和流产有一定相关,并表明流产次数增加,妊娠期亚临床甲减的发生率相应上升,和机体雌孕激素异常有关。本研究发现,流产次数 ≥ 2 次组妊娠期合并甲状腺功能异常发生率相对较高,但多因素发现其并非妊娠期甲状腺功能异常的独立影响因素,提示临床应加强对有既往流产史、反复流产史孕妇甲状腺功能的筛查。有关研究已证实甲状腺疾病发生情况和机体碘营养状态有关。其地区总体人群的碘营养状态无法准确反映本地妊娠期妇女的碘营养状态。研究表明,碘充足地区仍有大部分妊娠妇女发生碘缺乏,并表明碘营养状态和亚临床甲减发生率表现出"U"字型曲线。本研究结果显示,碘摄入量 $>150 \mu\text{g/d}$ 者甲状腺功能异常率较高,多因素分析发现碘摄入量 $>150 \mu\text{g/d}$ 是妊娠期甲状腺功能异常的独立危险因素。研究表明,香烟中的氰化物能够抑制碘吸收,推测妊娠期吸烟可能增加甲状腺功能疾病发生风险。本研究多因素分析显示吸烟并非是导致甲状腺功能异常的危险因素。

综上所述,加强对妊娠期妇女甲状腺功能的筛查和高危因素的管理能够预防不良妊娠结局,达到优生优育。

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