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妊娠糖尿病中肌肉/脂肪质量比与胰岛素抵抗的关系*

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摘要 目的:探究妊娠糖尿病中肌肉/脂肪质量比与胰岛素抵抗的相关性。**方法:**选择2015年1月至2020年1月于我院接受治疗的300例产妇为研究对象,按照美国糖尿病学会(American Diabetes Association,ADA)标准将产妇区分为妊娠期糖尿病组(GDM=90例)、妊娠期糖耐量受损组(GIGT=110例)和糖耐量正常组(NGT=100例),分别检测三组产妇的总胆固醇(total cholesterol,TC)、三酰甘油(Triglycerides,TG)、糖化血红蛋白(glycosylated hemoglobin,HbAlc)、肌肉/脂肪质量比(muscle/fat mass ratio,M/F)以及空腹血清胰岛素(fasting insulin,FINS)水平。**结果:**(1)GDM组患者HbAlc、TC以及TG水平均明显高于GIGT组以及NGT组(P<0.05),GIGT组患者HbAlc、TC以及TG水平均明显高于NGT组(P<0.05);(2)GMD组产妇的M/F明显低于GIGT组产妇,GIGT组产妇明显低于NGT组产妇(P<0.05),而GMD组产妇FINS以及胰岛素抵抗(insulin resistance,IR)明显高于GIGT组,GIGT组明显高于NGT组(P<0.05);(3)胰岛素抵抗(IR)同M/F呈现负相关联系(r=-0.218,P<0.05),同时与HbAlc、TC、TG(r=0.346,r=0.412,r=0.372,P<0.05)等呈现正相关。**结论:**妊娠女性的M/F值不足同胰岛素抵抗的出现具有一定的相关性,过分强调产妇节食可能会使产妇出现较低的肌肉质量,从而增加GDM的发生风险。

关键词:妊娠糖尿病;肌肉/脂肪质量比;胰岛素抵抗
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Relationship between Muscle / Fat Mass Ratio and Insulin Resistance in Gestational Diabetes*

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ABSTRACT Objective: To explore the relationship between muscle/fat mass ratio and insulin resistance in gestational diabetes mellitus. **Methods:** 300 pregnant women who were treated in our hospital from January 2015 to January 2020 were divided into gestational diabetes group (GDM=90 cases), gestational impaired glucose tolerance group (GIGT=110 cases) and normal glucose tolerance group (NGT=100 cases) according to the standards of American Diabetes Association (ADA). The total cholesterol (TC), triglyceride(TG), glycosylated blood red of the three groups were detected respectively Protein (HbAlc), muscle / fat mass ratio (M/F) and fasting serum insulin (fins) levels. **Results:** (1) The levels of HbAlc, TC and TG in GDM group were significantly higher than those in GIGT group and NGT group (P<0.05). The levels of HbAlc, TC and TG in GIGT group were significantly higher than those in NGT group (P<0.05). (2) The M/F of GMD group was significantly lower than that of GIGT group, and that of GIGT group was significantly lower than that of NGT group(P<0.05). In GMD group, fins and IR were significantly higher than those in GIGT group, GIGT group was significantly higher than NGT group (P<0.05). (3) IR was negatively correlated with M/F (r=- 0.218, P<0.05), at the same time, it was positively correlated with HbAlc, TC, TG (r=0.346, r=0.412, r=0.372, P<0.05). **Conclusion:** The insufficient M/F value of pregnant women was related to the occurrence of insulin resistance. Overemphasis on maternal diet may lead to lower muscle mass and increase the risk of GDM.

Key words: Gestational diabetes mellitus; Muscle/fat mass ratio; Insulin resistance
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前言

妊娠糖尿病是指患有糖尿病的患者妊娠,或者是女性妊娠前糖代谢正常,妊娠后出现糖尿病的现象,妊娠糖尿病会对母

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婴造成较大的影响，增加羊水过多、胎膜早破、新生儿窒息、巨大儿等[1-4]。数据统计，2017年国际糖尿病联盟(International Diabetes Federation，IDF)公布的地图数据显示，全球GDM发病率高达14.0 %[5]，我国GDM的发生率过去为1 %~5 %，而近几年的资料显示，GDM的发病率为1.7 %~16.7 %，有增加的趋势[6]，随着二胎政策的开放，妊娠糖尿病将会成为威胁母婴健康的重要因素。胰岛素抵抗是指因各种原因导致的胰岛素促进葡萄糖摄取和利用率降低，使机体产生高胰岛素血症[7,8]。临床实践发现，女性妊娠期间会出现生理性的胰岛素抵抗现象，且随着孕周的增加，胎盘会分泌多种激素如胎盘泌乳素、胎盘生长激素、糖皮质激素、孕激素等，上述激素会产生明显的胰岛素抵抗作用，导致机体对胰岛素的敏感性进一步降低[9,10]。近些年女性对于体重的认知较以往产生了明显的变化，部分产妇妊娠期间由于过度控制饮食导致其肌肉/脂肪质量比明显低于正常值。有调研发现此类产妇胰岛素抵抗强度明显增加，本研究旨在分析妊娠糖尿病产妇肌肉/脂肪质量比与其胰岛素抵抗之间的关系，以期为改善妊娠糖尿病产妇临床症状提供参考依据。

1 资料与方法

1.1 一般资料

选择2015年1月至2020年1月于我院接受治疗的300例产妇为研究对象，按照ADA标准将产妇分为妊娠期糖尿病组(GDM=90例)、妊娠期糖耐量受损组(GIGT=110例)和糖耐量正常组(NGT=100例)。纳入标准：(1)意识清晰能够配合调研；(2)病历资料齐全；(3)调研经本院医院伦理学会批准；(4)患者知情同意。排除标准：(1)合并精神疾患者；(2)非单胎产妇；(3)合并糖尿病史者；(4)合并全身慢性感染者；(5)调研依从性较差者；(6)合并妊娠期高血压者；(7)合并严重肝肾功能障碍者；(8)合并多囊卵巢综合征或胎膜早破者。

1.2 干预方法

1.2.1 临床资料收集 记录三组产妇的身高、孕前及分娩时的体质量，并计算其BMI，使用酶法检测三组产妇的TC、TG水平，并使用高效液相色谱法检测三组产妇的HbAlc水平。

1.2.2 血液指标检测 分别于分娩当日抽取空腹肘静脉血样5 mL，使用离心机以3000 r/min的速率离心10 min，留置血清置于-80 ℃条件下保存，待样本采集完毕后统一采用化学发光法检测FINS水平，并使用氧化酶法检测FPG水平，并按照IR=(FPG× FINS)/22.5计算胰岛素抵抗系数。

1.2.3 肌肉/脂肪质量比计算 使用东京Tanita公司生产的MC-190EM身体成分分析仪分别检测3组产妇的肌肉/脂肪质量比(M/F)，该分析仪主要用于测量孕妇身体组成，可以通过补偿子宫内的成分来计算受试者的M/F。

1.3 统计学方法

将采集的数据录入至SPSS 20.0软件中实施统计学分析，对于计量数据采取($\bar{x}\pm s$)表示，组间的差异性比较应用Student's t test检验，对于计量资料采取[n(%)]表示，采用卡方检验或F检验，P<0.05有统计学意义。

2 结果

2.1 三组产妇一般临床资料差异性比较

三组产妇的一般临床资料如平均年龄、平均产次、平均孕周等经过比较差异不具有统计学意义(F=0.012，0.106，0.115，P>0.05)，如表1所示。

表1 三组产妇一般临床资料比较($\bar{x}\pm s$)

Table 1 Comparison of general clinical data among three groups of parturients ($\bar{x}\pm s$)

Groups	n	Age (year)	birth time (time)	gestational week (week)
GDM	90	30.28±2.33	1.21±0.32	38.18±1.22
GIGT	110	30.31±2.29	1.22±0.29	38.11±1.23
NGT	100	30.33±2.01	1.23±0.29	38.18±1.21

2.2 三组产妇孕前及孕晚期体质量及BMI变化分析

三组产妇孕前体质量和BMI组间比较差异不具有统计学意义(P>0.05)，而孕晚期比较显示GDM组产妇的体质量明显高于GIGT组以及NGT组(P<0.05)，同时GIGT组明显高于NGT组(P<0.05)，GDM组产妇的体质量增加数明显高于GIGT组和NGT组(P<0.05)，如表2所示。

表2 三组产妇孕前及孕晚期体质量及BMI变化分析($\bar{x}\pm s$)

Table 2 Analysis of the changes of body mass and BMI in three groups ($\bar{x}\pm s$)

Groups	n	Progestational mass(kg)	Pre pregnancy BMI (kg/m^2)	Body weight in late pregnancy(kg)	Increase in body mass during pregnancy(kg)
GDM	90	64.33±3.22	23.29±3.21	83.28±8.11$^{\#*}$	18.29±4.33$^{\#*}$
GIGT	110	64.39±3.10	23.31±3.22	76.18±6.32$^{\#}$	16.01±3.22$^{\#}$
NGT	100	64.31±3.35	23.29±3.31	71.18±5.44	14.89±3.22
F	-	0.018	0.001	77.588	21.908
P	-	0.982	0.999	<0.001	<0.001

Note: Compared with NGT group, $^{\#}P$ <0.05, compared with GIGT group, * P <0.05.

2.3 三组产妇糖代谢指标差异性比较

GDM组患者HbAlc、TC以及TG水平均明显高于GIGT

组以及 NGT 组，经过比较存在统计学意义（P<0.05），GIGT 组患者 HbAlc、TC 以及 TG 水平均明显高于 NGT 组，经过比较存在统计学意义（P<0.05），如表 3 所示。

表 3 三组产妇糖代谢指标差异性比较（$\bar{x}\pm s$）

Table 3 Comparison of the differences in maternal glucose metabolism indexes among the three groups ($\bar{x}\pm s$)

Groups	n	HbAlc(%)	TC(mmol/L)	TG(mmol/L)
GDM	90	6.49±0.71#*	5.89±0.91#*	4.98±1.21#*
GIGT	110	6.01±0.32#	4.29±0.81#	3.21±0.71#
NGT	100	5.11±0.43	4.01±0.66	2.81±0.71
F	-	188.663	152.479	158.201
P	-	<0.001	<0.001	<0.001

Note: Compared with NGT group, #P<0.05, compared with GIGT group, * P<0.05.

2.4 三组产妇胰岛素抵抗及 M/F 差异性比较

GMD 组产妇的 M/F 明显低于 GIGT 组产妇，GIGT 组产妇明显低于 NGT 组产妇，经过比较存在统计学意义（P<0.05），而 GMD 组产妇 FINS 以及胰岛素抵抗（IR）明显高于 GIGT 组，GIGT 组明显高于 NGT 组，经过比较存在统计学意义（P<0.05），如表 4 所示。

表 4 三组产妇胰岛素抵抗及 M/F 差异性比较（$\bar{x}\pm s$）

Table 4 Comparison of maternal insulin resistance and M/F differences among the three groups ($\bar{x}\pm s$)

Groups	n	M/F	FINS(mIU/L)	IR
GDM	90	0.87±0.22#*	28.32±8.22#*	7.21±2.22#*
GIGT	110	0.91±0.23#	26.01±6.67#	5.51±0.98#
NGT	100	1.18±0.34	22.38±4.49	4.98±0.89
F	-	38.707	5.175	201.944
P	-	<0.001	0.018	<0.001

Note: Compared with NGT group, #P<0.05, compared with GIGT group, * P<0.05.

2.5 胰岛素抵抗与 M/F 相关性分析

经相关性分析显示，胰岛素抵抗（IR）同 M/F 呈现负相关（r=-0.218，P<0.05），同时与 HbAlc、TC、TG（r=0.346，r=0.412，r=0.372，P<0.05）等呈现正相关。

3 讨论

妊娠期糖尿病的发病率与地域存在较大关联，美国每年患病人次达 20 万，发病率为 7%，而在印度的发病率高达 19%[11,12]，而在我国 GDM 的发生率稍微较低，为 1.7 %~16.7 %。妊娠糖尿病的孕妇全身小血管均会出现不同程度的病变，其血管内腔细胞会增厚，导致组织供血不足，诱发妊娠高血压的发生，同时妊娠糖尿病还会损伤肝、肾等，诱发脑水肿、肝肾衰竭等，还可能会影响患者维生素 K 的吸收，诱发凝血功能障碍，增加产后出血的几率[13-15]，因而如何积极预防及治疗妊娠糖尿病是摆在医务工作者面前的一道难题。

近些年女性对于妊娠期间的体重管理越来越重视，甚至有部分女性在孕期过分强调控制体重而导致营养不良，影响胎儿的正常生长发育[16,17]，2016 年一项日本国家健康与营养调查结果显示，约有 11.9 %的日本女性存在体重不足的实际状况，尤其是育龄女性，20 岁左右的女性体重过轻的占比达 20.7 %，30 岁左右女性体重过轻的占比约为 16.8 %[18,19]。传统的研究认为，肥胖女性或预先存在胰岛素抵抗的女性发展为 GDM 的几率较高，但近些年的数据显示，一些非肥胖女性发展为 GDM 的几率也呈现逐年递增趋势[20,21]。国外有学者提出肌肉质量不足可能是诱发此类女性出现 GDM 的危险因素，同时也有研究指出肌肉组织不足会影响胰岛素信号通路和葡萄糖转运蛋白表达，进而增加 GDM 发生率，提示肌肉 / 脂肪质量当做影响胰岛素抵抗因素具有一定的理论基础[22,23]。

本研究通过设立不同分组的方式，就 GDM 患者中 M/F 与胰岛素抵抗之间的关系进行了探究，结果显示，相比于 GIGT 和 NGT 产妇，GDM 产妇的胰岛素分泌功能和 IR 指数均呈现明显升高现象。与高海侠[24]等学者的研究类似，发现与 NGT 组受试者相比，GDM 组及 GIGT 组均伴胰岛素功能、HOMA-IR 指数均显著升高，其中 GDM 组受试者升高幅度显著大于 GIGT 组，以往有研究指出，生理性的 IR 一定程度上有助于胎儿的营养师摄入，但对 GDM 产妇来说，胰岛素分泌能力升高，但是不会增加 IR，反而会降低外周组织对胰岛素敏感性，导致高血糖发生[25,26]。本文中 GDM 产妇的 FINS 以及 IR 均明显高于 NGT 产妇，提示 GDM 产妇存在高胰岛素血症以及 IR。此外文中还通过对三组产妇体质量进行了比较，以往的研究指出孕期体重增加过快、肥胖和超重是 GDM 的危险因素，文中对比结果提示 GDM 产妇体质量增加和 IR 明显高于 GIGT 组和 NGT 组产妇，与 Zhu W[27]等学者的研究类似，发现 GDM 组的体质量和 HOMA-IR 指数均显著高于 GIGT 组和 NGT 组产

妇,且 GIGT 组也高于 NGT 组产妇,分析其原因为肥胖或体重增加过快会导致脂肪细胞因子瘦素的过度表达,进而增加胰岛素抵抗现象,促进蛋白、脂肪的合成并抑制脂肪的分解,最终出现代谢紊乱,诱发 GDM 出现[28,29]。

最后文中还就三组产妇的 M/F 实施了组间差异性比较,并分析了 M/F 同 IR 之间的关联,结果显示 GDM 组产妇的 M/F 值明显低于 GIGT 组以及 NGT 组产妇。一项针对 20 例 GDM 产妇以及 20 例正产产妇的调研结果显示,GDM 产妇胰岛素受体底物、葡萄糖转运蛋白、葡萄糖转运蛋白 mRNA 在表达上存在明显的差异,此外还有研究指出,GDM 产妇肌肉组织中的磷脂酰肌醇 3 激酶和葡萄糖转运蛋白 4 同正常产妇相比明显发生变化[30,31]。本研究中通过组间比较以及相关性分析发现,GDM 产妇的 M/F 明显的要低于 GIGT 组以及 NGT 组产妇,相关性分析也提示 M/F 值同 IR 值存在明显的负相关性,分析其原因与肌肉量减小影响了产妇的葡萄糖代谢有关。有研究指出,胰岛素反应性运载体 - 葡萄糖载体蛋白 4 在维持机体葡萄糖运转系统中起到关键性作用,数据显示 GDM 产妇脂肪组织中葡萄糖载体蛋白 4 的表达会下降约 40 %,提示骨骼肌量的减小会影响葡萄糖载体蛋白 4 的表达,导致葡萄糖转运障碍的发生[32,33]。进一步的相关性分析则指出 M/F 同 IR 存在明显相关性,也印证了上述论点。目前对于 GDM 产妇的 M/F 值的研究还很少,需要在本研究的基础上深入探究妊娠女性的 M/F 值与胰岛素抵抗的相关性,为 GDM 的预防和治疗提供思路。

综上所述,妊娠女性的 M/F 值不足同胰岛素抵抗的出现具有一定的相关性,过分强调产妇节食可能会使产妇出现较低的肌肉质量,从而增加 GDM 的发生风险。

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