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·临床研究·

妊娠期糖尿病患者氧化应激水平变化及临床意义*

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摘要 目的：研究 GDM 孕妇与正常孕妇血清 MDA、SOD 及 GSH 水平变化，探索它们与 GDM 之间的相互关系，追踪各组妊娠结局研究其临床意义。**方法：**选取 175 例孕妇为研究对象，分为 GDM 组 (93 例) 和对照组 (82 例)。采用微量法测定血清丙二醛 (MDA)、谷胱甘肽（GSH）及超氧化物歧化酶（SOD）水平，并对妊娠结局进行相关性分析。**结果：**(1) GDM 组年龄、孕前体重、BMI 值均高于对照组，GSH 和 SOD 水平均低于对照组，MDA 水平高于对照组，差异有统计学意义（*P<0.05*）；(2) GDM 组 MDA 水平与孕前体重呈负相关（r=-0.3547，*P<0.05*），SOD 水平与新生儿出生体重呈正相关（r=0.3292，*P<0.05*），SOD 值与早产之间有密切联系（足月产 12.68 ± 0.85 vs. 早产 8.08 ± 1.18, *P < 0.05*），GSH、SOD 水平与孕前体重之间，MDA、GSH 水平与新生儿出生体重之间，MDA、GSH 水平与早产之间均无明显相关性（*P>0.05*），MDA、GSH 和 SOD 水平与剖宫产及胎膜早破均无明显相关性（*P>0.05*）。**结论：**GDM 存在明显的氧化应激反应，GSH、MDA 与 SOD 可以作为评估 GDM 氧化应激的有效标志物，其与不良妊娠结局有关。

关键词：妊娠期糖尿病；氧化应激；丙二醛；谷胱甘肽；超氧化物歧化酶

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Changes in Biomarkers of Oxidative Stress and Their Clinical Significance in Gestational Diabetes Mellitus*

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ABSTRACT Objective: To investigated changes in malondialdehyde (MDA), glutathione (GSH), or superoxide dismutase (SOD) and their relationship with pregnancy outcomes in patients with GDM to evaluate their clinical significance. **Methods:** The study included 2 groups of pregnant women (GDM and healthy controls). Oxidative stress biomarkers were evaluated by absorbance-based assay, and all patients' pregnancy outcomes were tracked. **Results:** In the GDM group, women were older, had a higher prepregnancy weight, a higher BMI value, delivered at earlier gestational weeks, Women with GDM showed increased levels of MDA and reduced expression levels of GSH and SOD compared with control group. In the GDM group, MDA levels were negatively associated with prepregnancy weight, and SOD levels were positively correlated with neonatal birth weight. We found an intensive relationship between SOD content and preterm birth in the GDM group. Moreover, prepregnancy weight don't associated with GSH and SOD levels. There is no significant difference between the level of MDA/GSH and neonatal birth weight as well as preterm birth. MDA, GSH, and SOD levels were not associated with an increased risk of cesarean delivery or PROM. **Conclusion:** This study indicates there is oxidative stress in GDM. and the changes in biomarkers we measured are associated with adverse pregnancy outcomes.

Key words: Oxidative stress; GDM; GSH; SOD; MDA

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前言

妊娠期糖尿病(Gestational diabetes mellitus,GDM)是指娠期发生或首次被发现的糖尿病,有别于 I 型糖尿病和 II 型糖尿病 [1]。在全球范围内 GDM 发病率为 2%—14%[2,3], 在中国为 2.4%到 6.8%[4],并且逐年增长。

GDM 孕妇易出现子痫前期、早产、剖宫产、巨大儿等并发症[5],且易发生流产、胎膜早破等异常情况,此外,GDM 患者子代患肥胖症及 II 型糖尿病的风险更高[6]。GDM 及其并发症的发生及发展可能与氧化和抗氧化系统之间的不平衡密切相关。GDM 孕妇表现出过度糖化从而引起氧化应激及抗氧化酶减少[7],氧化应激的增加可能会对母体和胎儿都产生不利影响[8]。丙二醛(MDA)是脂质氧化终产物,可以引起磷脂降解从而产生一系列病变,如糖尿病[9],常用来了解膜脂过氧化程度及氧化应激情况[10]。还原型谷胱甘肽(GSH)是最常用的抗氧化剂之一。研究发现,与健康孕妇相比,患有糖尿病的孕妇血液中 GSH 含量明显降低, 这表明氧化应激的增加 [11]。超氧化物歧化酶(SOD)是生物体内重要的抗氧化酶,可以清除氧自由基及抑制氧化应激 [12], 患 GDM 孕妇肝脏组织中的 SOD 活性显著下降[13]。因此,评估 GDM 患者氧化应激水平具有重要意义,本研究旨在通过对 GDM 孕妇与正常孕妇血清 MDA、SOD 及 GSH 的研究,探索它们与 GDM 的相互关系,并且追踪各组妊娠结局研究其临床意义以减少不良围产结局发生。

1 材料与方法

1.1 一般资料

本实验选取了在松江区妇幼保健院建卡产检的 175 名年龄在 21 岁到 41 岁之间的孕妇。所有孕妇根据血糖值分为两组:(1)93 例妊娠期糖尿病孕妇(GDM 组)和(2)82 名健康孕妇(对照组)。孕妇患有其他合并症如妊娠期高血压、子痫前期、甲状腺功能减退或胎盘早剥等都被排除在外,患 GDM 需要胰岛素治疗的孕妇也被排除在外。妊娠期糖尿病的诊断基于美国糖尿病协会的标准 [14], 即在孕 24 至 28 周行 75 g 口服葡萄糖耐量试验 (OGTT), 血糖符合下列标准之一的孕妇即被诊断为 GDM:空腹血糖≥ 5.1 mmol/L;餐后 1 h 血糖≥ 10.0 mmol/L;餐后 2 h 血糖≥ 8.5 mmol/L。

1.2 实验方法

1.2.1 **标本采集** 当入组孕妇进行 OGTT 试验时, 抽取静脉血,吸出血清置入离心管中,转存至上海市第一人民医院南院 -80℃ 冰箱中,备氧化应激指标测定。随后追踪所有孕妇的妊娠结局,GDM 组中死胎 1 例,流产 1 例,失访 14 例,对照组中失访 17 例。故最终入组 142 例(GDM 组 77 例,对照组 65 例)。

1.2.2 **检测方法** (1)GSH 的测定:GSH 试剂盒为上海索桥生物公司提供。酶标仪(Thermo Scientific Varioskan Flash)预热 30 min,调节波长至 412 nm。试剂二置于 25℃ 水浴中保温 30 min。空白管:96 孔板依次加入 20 μL 蒸馏水,140 μL 试剂二,40 μL 试剂三,混匀静置 2 min,后测定 412 nm 吸光度 A1。测定管中步骤相同,仅将蒸馏水改为血清,后测定 412 nm 吸光度 A2。最后按照公式 GSH(μmol/mL)=6.67× (A2-A1)计算出最终值。

(2)SOD 的测定:SOD 试剂盒为上海索桥生物公司提供。在测定管中依次加入试剂一 45 μL, 试剂二 100 μL, 试剂三 2 μL,血清 18 μL,试剂四 35 μL,对照管中重复上述步骤,仅将血清改为双蒸水,加样量相同。充分混匀,室温静置 30 min 后,用酶标仪波长 560 nm 处测定各管吸光值 A。按照说明书公式计算出 SOD 值(U/mL)。

(3)MDA 的测定:MDA 试剂盒为上海索桥生物公司提供。吸取 0.3 mL 试剂一于 1.5 mL 离心管中, 再加入 0.1 mL 血清,混匀。95℃ 水浴中保温 30 min,置于冰浴中冷却,然后 10000× g 离心力,25 ℃ ,离心 10 min。吸取 200 μL 上清液于 96 孔板中,测定 532 nm 和 600 nm 处的吸光度。按照说明书公式计算出 MDA 值(nmol/mL)。

1.3 统计学分析

应用 SAS9.1 及 GraphPad Prism5 软件进行统计,计量数据采用均数± 标准误(mean ± SEM)以及均数± 标准差(mean ± SD)表示,计量资料采用 t 检验,卡方检验,相关分析应用皮尔森相关系数分析。$p<0.05$ 为显著性检验标准,有统计学意义。

2 结果

2.1 两组孕妇一般临床特点

与对照组相比,GDM 组年龄更大, 孕前体重更高,BMI 指数更高,且分娩孕周更早($P<0.05$)见表 1。

表 1 GDM 组孕妇与对照组孕妇一般临床特点

Table 1 Clinical characteristics of pregnant women from the GDM (n = 77) and control (n = 65) groups

Groups	Age (year)	Prepregnancy weight (kg)	BMI (kg/m^2)	Gestational weeks at delivery(week)
GDM	31.32 ± 0.53	56.49 ± 0.95	22.15 ± 0.36	38.43 ± 0.25
Control	28.62 ± 0.50	52.44 ± 0.80	20.45 ± 0.30	39.35 ± 0.12
t	3.658	3.170	3.541	3.099
P	0.0004*	0.0019*	0.0005*	0.0024*

2.2 两组孕妇妊娠结局比较

两组在剖宫产率、巨大儿发生率、胎膜早破率、早产率比较差异均无统计学意义 ($P>0.05$), 见表 2。

2.3 两组孕妇氧化标志物变化

如图 1 所示,GDM 组 MDA 水平显著高于对照组((1.16 ± 0.17 vs. 0.74 ± 0.33 nmol/mL, $P < 0.05$),而 GSH 值及 SOD值则显著低于对照组 (2.09 ± 0.06 vs. 2.3 ± 0.06 μmol/mL, $P < 0.05$; 图 2) (11.87 ± 0.78 vs. 14.31 ± 0.86 U/mL, $P < 0.05$; 图 3)。

表 2 GDM 组孕妇与对照组孕妇妊娠结局比较

Table 2 Comparison of pregnancy outcomes between the GDM and control groups, n (%)

Groups	Cesarean delivery	Macrosomia	PROM	Preterm
GDM	40 (51.95%)	8 (10.39%)	14 (18.18%)	6 (7.79%)
Control	24 (36.92%)	2 (3.08%)	8 (12.31%)	1 (1.54%)
x^2	3.214	2.879	0.929	2.941
P	0.073	0.090	0.335	0.086

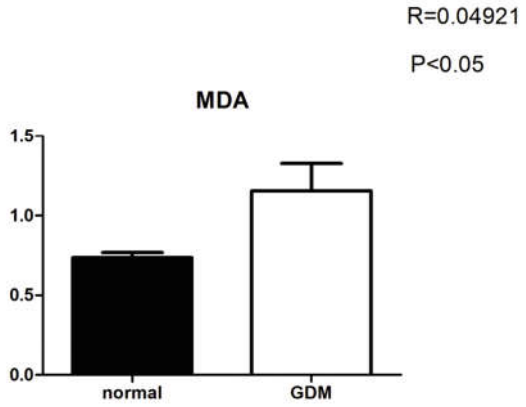

图 1 GDM 组与对照组 MDA 水平变化

Fig.1 MDA level in serum of GDM and healthy pregnancies

Note: Data are given as the mean ± SEM. Statistical significance was determined using an independent t test. t = 2.643, *P* = 0.0092. MDA, malondialdehyde; GDM, gestational diabetes mellitus.

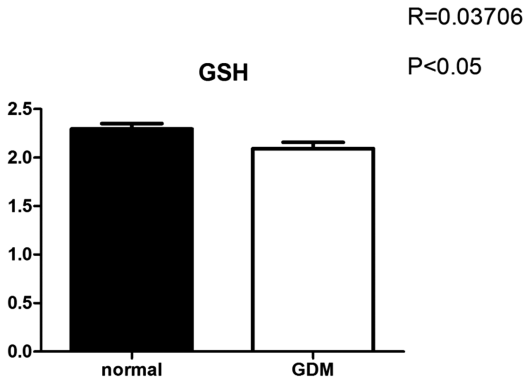

图 2 GDM 组与对照组 GSH 水平变化

Fig.2 GSH level in serum of GDM and healthy pregnancies

Note: Data are given as the mean ± SEM. Statistical significance was determined using an independent t test. t = 2.321, *P* = 0.0217. GSH, glutathione; GDM, gestational diabetes mellitus.

2.4 GDM 组中氧化应激与妊娠结局相关分析

在 GDM 组中氧化应激标记物的变化与妊娠结局有显著关联。MDA 水平与孕前体重呈负相关(r=-0.3547,*P<0.05*),而 GSH、SOD 水平同孕前体重之间没有明显的相关性（*P>0.05*）(图 4)。SOD 水平与新生儿出生体重呈正相关（r=0.3292,*P<0.05*),MDA 和 GSH 水平与新生儿出生体重无明显相关性(*P>0.05*)(图 5)。与此同时,我们发现血清 SOD 值与早产之间有密切联系(足月产 12.68 ± 0.85 vs.早产 8.08 ± 1.18, *P < 0.05*),MDA、GSH 水平与早产之间没有显著关联（*P>0.05*)(图 6)。MDA、GSH 和 SOD 水平与剖宫产及胎膜早破均无明显相关性(*P>0.05*)(图 7-8)。

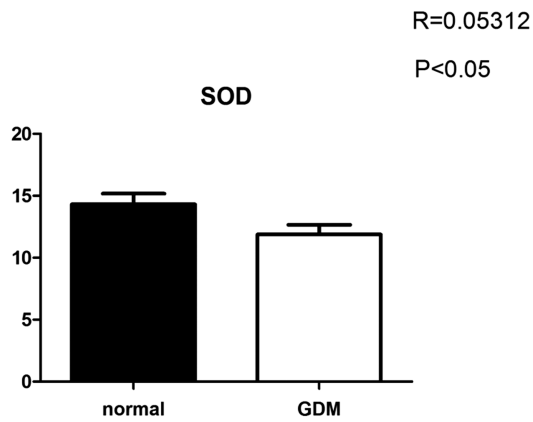

图 3 GDM 组与对照组 SOD 水平变化

Fig.3 SOD level in serum of GDM and healthy pregnancies

Note: Data are given as the mean ± SEM. Statistical significance was determined using an independent t test. t = 2.092, *P* = 0.0397. SOD, superoxide dismutase; GDM, gestational diabetes mellitus.

3 讨论

氧化应激是指体内氧化与抗氧化作用失衡,可以导致组织损伤。虽然 GDM 确切的发病机制还不清楚,但氧化应激在其中发挥着重要的作用[15]。在本研究中,GDM 患者 MDA 水平增高与诸多研究一致[16]。SOD 与 GSH 是生物体内重要的抗氧化酶,本实验结果表明在 GDM 患者中 SOD 水平与 GSH 水平显著下降,Samar Sultan 等人也同样证明了在 GDM 中 SOD 水平是下降的[17]。既往对 GDM 患者的研究均表明当氧化应激水平增强时,抗氧化防御功能下降[7]。

本研究表明，在 GDM 组孕妇孕前体重显著高于对照组，且MDA 水平与孕前体重呈正相关。同时,GDM 组中巨大儿发生率为 10.39%,高于对照组(3.08%)。而大多数研究证明 GDM 患者无论是否生育巨大儿，发生不良围产结局的风险均增加，包括胎死宫内、新生儿死亡、肩难产、子痫前期[18]。本实验还表明 SOD 水平与新生儿出生体重有关联。Oussama 等人也发现 GDM 患者生育巨大儿与 SOD 活性有关。在全球范围内,与对照组相比,GDM 患者及其巨大儿的血清抗氧化防御能力都有所下降 [19]。为了证明上述观点,Meriem 等人发现红细胞 SOD 水平在大于胎龄儿中是显著增加的。这些数据都证明在巨大儿中确实存在氧化应激失衡[20]。本研究并没有发现 MDA 水平与新生儿出生体重有关系,这与我们预期结果并不相符,因为过去的一项研究证明患有宫内生长发育迟缓(IUGR)的孕妇,其

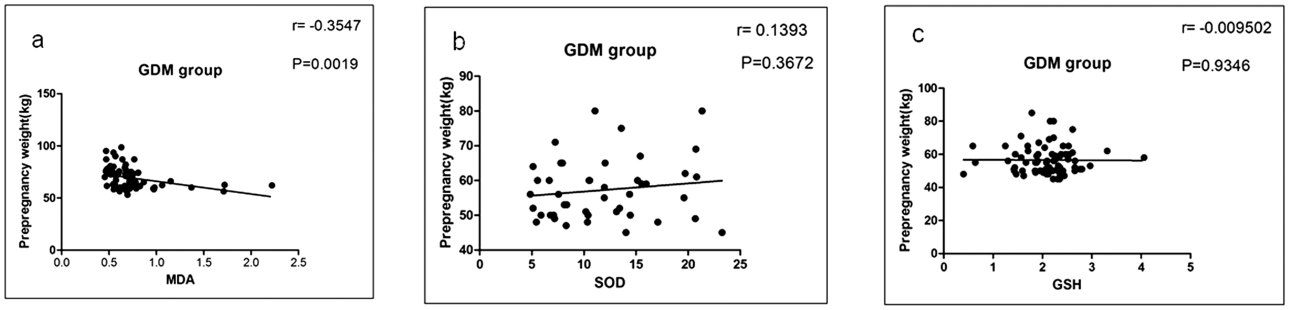

图 4 GDM 组中 MDA、SOD 与 GSH 水平与孕前体重关系

Fig.4 Relationship between MDA, SOD, and GSH levels and prepregnancy weight in the GDM group

注:相关分析应用皮尔森系数相关分析。(a)MDA 水平与孕前体重呈负相关 r = -0.3547, *P* = 0.0019。(b)SOD 水平与孕前体重无明显相关性 r = 0.1393, *P* = 0.3672。(c)GSH 水平与孕前体重无明显相关性 r = -0.009502, *P* = 0.9346。MDA,丙二醛;SOD, 超氧化物歧化酶;GSH, 谷胱甘肽;GDM, 妊娠期糖尿病。

Note: Statistical significance was determined using Pearson correlation coefficient analysis. (a) Relationship between MDA and prepregnancy weight in the GDM group. r = -0.3547, *P* = 0.0019. (b) Relationship between SOD and prepregnancy weight in the GDM group. r = 0.1393, *P* = 0.3672. (c) Relationship between GSH and prepregnancy weight in the GDM group. r = -0.009502, *P* = 0.9346. MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione; GDM, gestational diabetes mellitus.

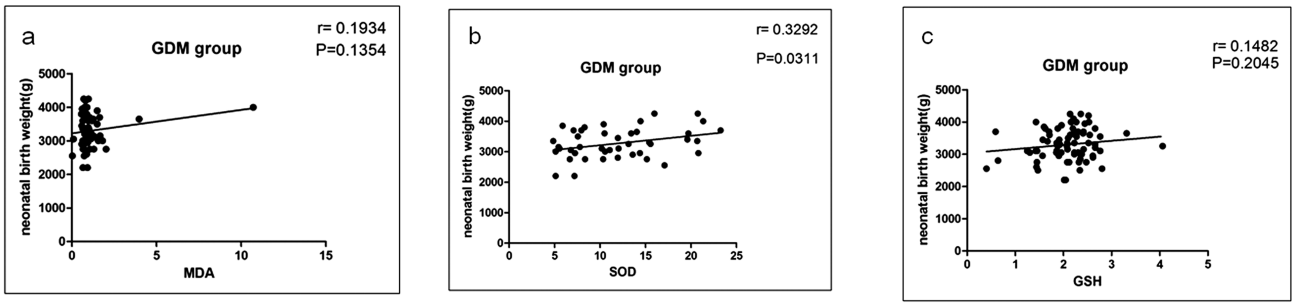

图 5 GDM 组中 MDA、SOD 与 GSH 水平与新生儿出生体重关系

Fig.5 Correlation between MDA, SOD, and GSH levels and neonatal birth weight in the GDM group

注:相关分析应用皮尔森系数相关分析。(a)MDA 水平与新生儿出生体重无明显相关性 r = 0.1934, *P* = 0.1354。(b)SOD 水平与新生儿出生体重成正相关 r = 0.3292, *P* = 0.0311。(c)GSH 水平与新生儿体重无明显相关性 r = 0.1482, *P* = 0.2045。MDA,丙二醛;SOD, 超氧化物歧化酶;GSH, 谷胱甘肽;GDM, 妊娠期糖尿病。

Note: Statistical significance was determined using Pearson correlation coefficient analysis. (a) The correlation between MDA and neonatal birth weight in the GDM group. r = 0.1934, *P* = 0.1354. (b) The correlation between SOD and neonatal birth weight in the GDM group. r = 0.3292, *P* = 0.0311. (c) The correlation between GSH and neonatal birth weight in the GDM group. r = 0.1482, *P* = 0.2045. MDA, malondialdehyde; SOD: superoxide dismutase; GSH: glutathione; GDM: gestational diabetes mellitus.

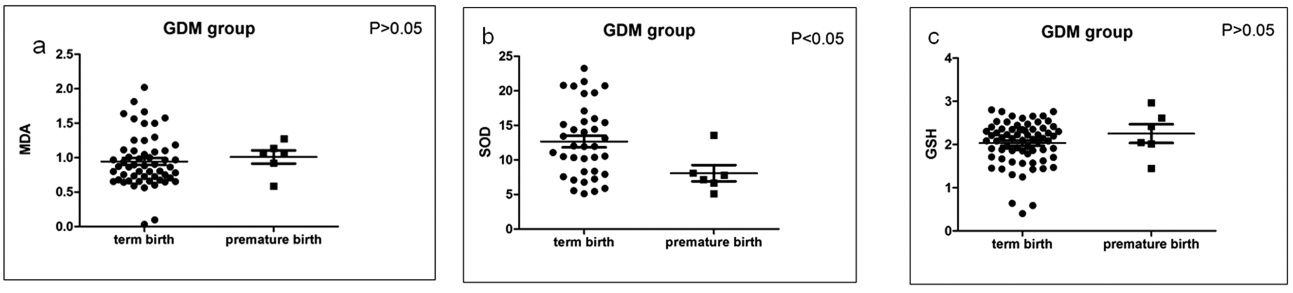

图 6 GDM 组中 MDA、SOD 与 GSH 水平与早产之间的关系

Fig.6 Comparison of MDA, SOD, and GSH values between term birth and premature birth in the GDM group

注:数据分析采用非配对 t 检验。(a)MDA 水平与早产率无明显相关性 t = 0.4000, *P* = 0.6906。(b)SOD 水平与早产率成正相关 t = 2.113, *P* = 0.0407。(c)GSH 水平与早产率无明显相关性 t =1.030, *P* = 0.3064。MDA,丙二醛;SOD, 超氧化物歧化酶; GSH, 谷胱甘肽; GDM,妊娠期糖尿病。

Note: Data are given as the mean ± SEM. Statistical significance was determined using an unpaired t test. (a) Comparison of MDA value between term birth and premature birth in the GDM group. t = 0.4000, *P* = 0.6906. (b) Comparison of SOD value between term birth and premature birth in the GDM group. t = 2.113, *P* = 0.0407. (c) Comparison of GSH value between term birth and premature birth in the GDM group. t =1.030, *P* = 0.3064. MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione; GDM, gestational diabetes mellitus.

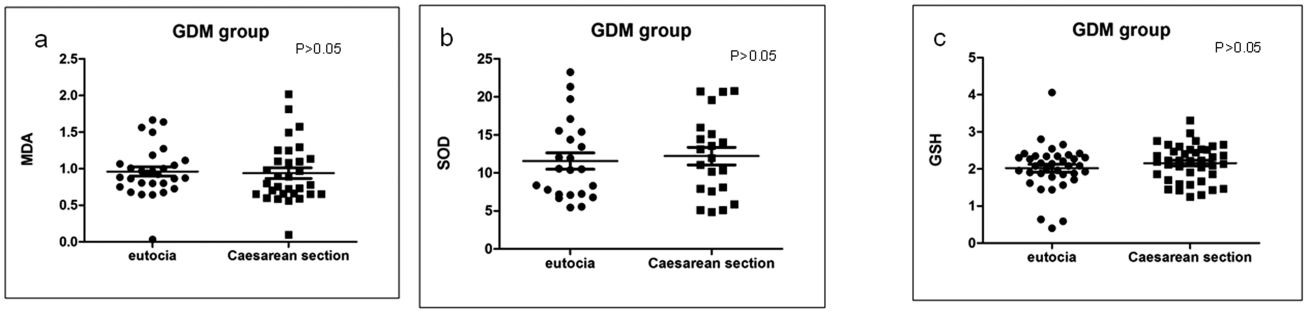

图 7 GDM 组中 MDA、SOD 与 GSH 水平与剖宫产之间的关系

Fig.7 Comparison of MDA, SOD, and GSH values between eutocia and cesarean delivery in the GDM group

注:数据分析采用非配对 t 检验。(a)MDA 水平与剖宫产率无明显相关性 t = 0.2430, *P* = 0.8088。(b)SOD 水平与剖宫产率无明显相关性 t = 0.4065, *P* = 0.6865。(c)GSH 水平与剖宫产率无明显相关性 t = 1.066, *P* = 0.2898。MDA,丙二醛; SOD, 超氧化物歧化酶; GSH, 谷胱甘肽; GDM, 妊娠期糖尿病。

Note: Data are given as the mean ± SEM. Statistical significance was determined using an unpaired t test. (a) Comparison of MDA value between eutocia and cesarean delivery in the GDM group. t = 0.2430, *P* = 0.8088. (b) Comparison of SOD value between eutocia and cesarean delivery in the GDM group. t = 0.4065, *P* = 0.6865. (c) Comparison of GSH value between eutocia and cesarean delivery in the GDM group. t = 1.066, *P* = 0.2898. MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione; GDM, gestational diabetes mellitus.

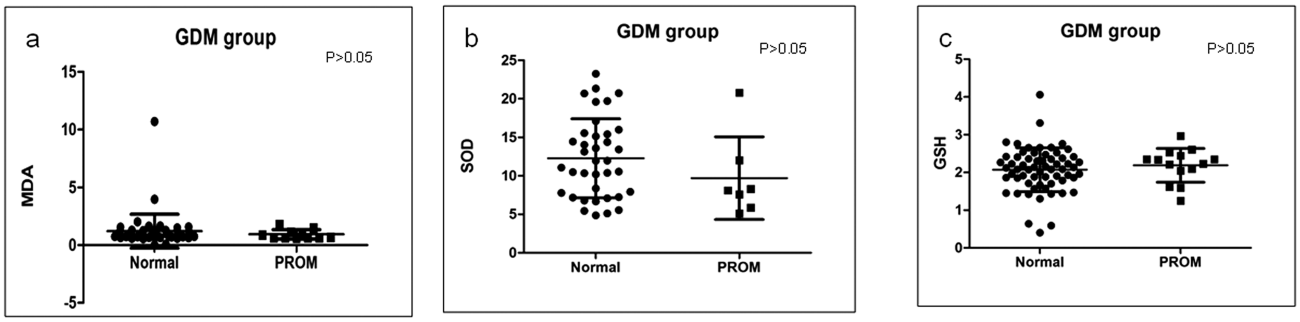

图 8 GDM 组中 MDA、SOD 与 GSH 水平与胎膜早破之间的关系

Fig.8 Comparison of MDA, SOD, and GSH values between healthy women and those with PROM in the GDM group

注:数据分析采用非配对 t 检验。(a)MDA 水平与胎膜早破率无明显相关性 t = 0.5893, *P* = 0.5579。(b)SOD 水平与胎膜早破率无明显相关性. t = 1.217, P = 0.2304。(c)GSH 水平与胎膜早破率无明显相关性 t = 0.6967, *P* = 0.4882。MDA,丙二醛;SOD, 超氧化物歧化酶; GSH, 谷胱甘肽; GDM, 妊娠期糖尿病。

Note: Data are given as the mean ± SEM. Statistical significance was determined using an unpaired t test. (a) Comparison of MDA value between healthy and PROM in the GDM group. t = 0.5893, *P* = 0.5579. (b) Comparison of SOD value between healthy and PROM in the GDM group. t = 1.217, *P* = 0.2304. (c) Comparison of GSH value between healthy and PROM in the GDM group. t = 0.6967, *P* = 0.4882. MDA, malondialdehyde; SOD, superoxide dismutase; GSH, glutathione; GDM, gestational diabetes mellitus; PROM, premature rupture of membranes.

羊水中 MDA 的浓度明显高于健康孕妇，并且 MDA 的检测对于 IUGR 有诊断意义[21],造成这种不同结果的原因可能是本实验测定的是血清 MDA 含量,而非羊水中的 MDA 含量。本研究还发现在 GDM 组中 SOD 含量与早产有密切关联。Maqusood 等人也发现早产孕妇胎盘组织中 SOD 的含量远高于足月产孕妇[22],这与我们的研究结果一致。Pathak 等人证明与足月产孕妇相比,早产孕妇的血 MDA 水平明显提高[23]。然而本实验的结论是 MDA 值与早产无明显相关性,这可能与早产的样本量较少有关系，因此还需要进一步研究。本研究发现 GDM 组剖宫产、巨大儿、早产、胎膜早破发生率都高于对照组,这与大多数研究一致[24,25]。我们的结果表明 GSH、MDA 与 SOD 值均与剖宫产没有显著关联,这可能与社会因素及前次剖宫产数量逐年增加有关。

综上所述,GDM 存在明显的氧化应激反应,GSH、MDA 与 SOD 可以作为评估 GDM 氧化应激的有效标志物。这些标志物与母体体重及妊娠结局密切相关,因此提示医生在孕期不仅需要监测血糖和控制体重,而且应该监测 GDM 中氧化应激水平的变化。因此,我们建议对 GDM 的氧化及抗氧化状态进行后续研究,以减少不良围产结局发生。

参 考 文 献(References)

[1] American Diabetes Association, Standards of medical care in diabetes [J]. Diabetes Care, 2016, 39: S13-S22

[2] J M Lawrence. Women with diabetes in pregnancy: different perceptions and expectations, Best Pract [J]. Res Clin Obstet Gynaec, 2011, 25: 15-24

[3] Carolan M, Davey MA, Biro MA, et al. Maternal age, ethnicity and gestational diabetes mellitus[J]. Midwifery, 2012, 28(6): 778-783

[4] Zhang F, Dong L, Zhang C P, et al. Increasing prevalence of gestational diabetes mellitus in Chinese women from 1999 to 2008[J]. Diabetic medicine: a journal of the British Diabetic Association, 2011, 28(6): 652-657

[5] Lamiaa Mohsen, Dina M. Akmal, Elsayed Kamal Elsayed Ghonaim, et al. Role of mean platelet volume and ischemia modified albumin in evaluation of oxidative stress and its association with postnatal complications in infants of diabetic mothers [J]. The Journal of Maternal-Fetal & Neonatal Medicine, 2018, 31(14): 1819-1823

[6] Antonino Santacroce, Giuseppe De Bernardo, Simona Negro, et al. Diabetes or Obesity in Pregnancy and Oxidative Stress in the Offspring[J]. J Pediatr Biochem, 2016, 6: 92-95

[7] Lappas M, Hiden U, Desoye G, et al. The role of oxidative stress in the pathophysiology of gestational diabetes mellitus [J]. Antioxid Redox Signal, 2011, 15: 3061-3100

[8] Sultan Samar, Alzahrani Nada, Al-Sakkaf Kalthoom. The postpartum effect of maternal diabetes on the circulating levels of sirtuins and superoxide dismutase[J]. FEBS open bio, 2018, 8: 2

[9] Bhutia Y, Ghosh A, Sherpa ML, et al. Serum malondialdehyde level: surrogate stress marker in the Sikkimese diabetics [J]. J Nat Sci Biol Med, 2011, 2: 107

[10] Nielsen F, Mikkelsen BB, Nielsen JB, et al. Plasma malondialdehyde as biomarker for oxidative stress: reference interval and effects of life-style factors[J]. Clin. Chem, 1997, 43(7): 1209-1214

[11] Kharb S. Low whole blood glutathione levels in pregnancies complicated by preeclampsia and diabetes[J]. Clin. Chim. Acta, 2000, 294(1): 179-183

[12] Min Shang, Junpeng Zhao, Lei Yang, et al. Oxidative stress and antioxidant status in women with gestational diabetes mellitus diagnosed by IADPSG criteria [J]. Diabetes Research and Clinical Practice, 2015, 109(2): 404-410

[13] Zhaohui Zeng, Yun Xu, Bin Zhang. Antidiabetic Activity of a Lotus Leaf Selenium (Se)-Polysaccharide in Rats with Gestational Diabetes Mellitus[J]. Biological Trace Element Research, 2017, 176 (2): 321-327

[14] American Diabetes Association, Diagnosis and classification of diabetes mellitus[J]. Diabetes Care, 2014, 37(1): S81-S90

[15] Zein S, Rachidi S, Hininger-Favier I. Is oxidative stress induced by iron status associated with gestational diabetes mellitus?[J]. J Trace Elem Med Biol, 2014, 28(1): 65-69

[16] Arribas L, Almansa I, Miranda M, et al. Serum malondialdehyde concentration and glutathione peroxidase activity in a longitudinal study of gestational diabetes[J]. PLoS One, 2016, 11(5): e0155353

[17] Samar Sultan, Nada Alzahrani, Kalthoom AlSakkaf. The postpartum effect of maternal diabetes on the circulating levels of sirtuins and superoxide dismutase[J]. FEBS Open Bio, 2018, 8(2): 256-263

[18] Kwik M, Seeho SK, Smith C, et al. Outcomes of pregnancies affected by impaired glucose tolerance[J]. Diabetes Res Clin Pract, 2007, 77: 263-268

[19] Oussama Grissa, Jean-Marc Atègbo, Akadiri Yessoufou, et al. Antioxidant status and circulating lipids are altered in human gestational diabetes and macrosomia [J]. Translational Research, 2007, 150(3): 164-171

[20] Meriem Saker, Nassima Soulimane Mokhtari, Sid Ahmed Merzouk, et al. Oxidant and antioxidant status in mothers and their newborns according to birthweight [J]. European Journal of Obstetrics and Gynecology, 2008, 141(2): 95-99

[21] Bazowska G, Jendryczko A. Concentration of malondialdehyde (MDA) in amniotic fluid and maternal and cord serum in cases of intrauterine growth retardation[J]. Zentralbl Gynakol, 1994, 116: 329-330

[22] Maqusood Ahamed, Prateek Kumar Mehrotra, Prabhat Kumar, et al. Placental lead-induced oxidative stress and preterm delivery [J]. Environmental Toxicology and Pharmacology, 2009, 27(1): 70-74

[23] Pathak R, Suke SG, Ahmed T, et al. Organochlorine pesticide residue levels and oxidative stress in preterm delivery cases [J]. Hum Exp Toxicol, 2010, 29(5): 351-358

[24] Cosson E, Cussac-Pillegand C, Benbara A, et al. Pregnancy adverse outcomes related to pregravid body mass index and gestational weight gain, according to the presence or not of gestational diabetes mellitus: A retrospective observational study [J]. Diabetes Metab, 2016, 42(1): 38-46

[25] Cécile Billionnet, Delphine Mitanchez, Alain Weill, et al. Gestational diabetes and adverse perinatal outcomes from 716,152 births in France in 2012[J]. Diabetologia, 2017, 60(4): 636-644

·重要信息·

《现代生物医学进展》2019 年封面设计说明

此版封面的主体为肿瘤细胞与效应 T 细胞，并特别突出显示了肿瘤细胞表面所表达的免疫抑制受体 PD-L1。众所周知，2018 年诺贝尔生理学或医学奖授予了美国科学家詹姆斯·艾利森和日本科学家庶佑，以表彰他们所发现的抑制免疫负调节的癌症疗法——“免疫检查点疗法”，而 PD-1/PD-L1 通路正是该疗法所针对的一条十分重要的免疫抑制性信号通路。近年来，新兴的肿瘤免疫疗法蓬勃发展，PD-1/PD-L1 抑制剂作为其重要代表，一经问世就朝着靶向治疗，精准治疗的方向不断前行，为癌症治疗开创了全新的免疫治疗思路。

2019 年度杂志封面选择新型的肿瘤免疫疗法为主题，紧跟诺贝尔获奖热点，所表现内容辨识度高，符合《现代生物医学进展》的办刊主旨和特色。