

doi: 10.13241/j.cnki.pmb.2022.12.024

多囊卵巢综合征肥胖患者血清维生素 D、铁蛋白水平、sICAM-1 与胰岛素抵抗、糖脂代谢指标的相关性 *

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摘要 目的:探讨多囊卵巢综合征(PCOS)肥胖患者血清维生素 D、铁蛋白、可溶性细胞间粘附分子-1(sICAM-1)水平与胰岛素抵抗、糖脂代谢指标的相关性。**方法:**2018 年 8 月到 2021 年 11 月,选择在本院妇科诊治的 PCOS 患者 65 例作为研究对象,分为 PCOS 肥胖组($n=30$,体重指数 $\geq 28 \text{ kg/m}^2$)和 PCOS 非肥胖组($n=35$,体重指数 $<28 \text{ kg/m}^2$)。检测与计算两组血清维生素 D、铁蛋白、sICAM-1、胰岛素抵抗、糖脂代谢指标并进行相关性分析。**结果:**两组的血清甲状腺素(T₄)、促甲状腺激素(TSH)与泌乳素(PRL)对比差异无统计学意义($P>0.05$),肥胖组的血清促黄体生成素(LH)、促卵泡生成素(FSH)、睾酮(T)水平高于非肥胖组($P<0.05$)。肥胖组的血清铁蛋白、sICAM-1 水平高于非肥胖组,血清维生素 D 水平低于非肥胖组($P<0.05$)。肥胖组的胰岛素抵抗指数(HOMA-IR)、胰岛素水平(FINS)、甘油三酯(TG)、总胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)较非肥胖组,高密度脂蛋白胆固醇(HDL-C)低于非肥胖组($P<0.05$)。在 PCOS 肥胖患者中,Pearson 分析显示血清维生素 D、铁蛋白、sICAM-1 与胰岛素抵抗、糖脂代谢指标都存在相关性($P<0.05$)。**结论:**PCOS 肥胖患者与非肥胖患者的血清维生素 D、铁蛋白、sICAM-1、胰岛素抵抗、糖脂代谢指标水平存在差异,血清维生素 D、铁蛋白、sICAM-1 水平与胰岛素抵抗、糖脂代谢指标存在相关性。

关键词:多囊卵巢综合征;维生素 D;铁蛋白;可溶性细胞间粘附分子-1;胰岛素抵抗;糖脂代谢

中图分类号:R588.6;R711.75 **文献标识码:**A **文章编号:**1673-6273(2022)12-2318-04

Correlation of Serum vitamin D, Ferritin levels, sICAM-1 with Insulin Resistance, Glucose and Lipid Metabolism Indexes in Obese Patients with Polycystic Ovary Syndrome*

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ABSTRACT Objective: To investigate the relationship between serum vitamin D, ferritin, and sICAM-1 levels in obese patients, who has polycystic ovary syndrome and insulin resistance, glucose and lipid metabolism indexes sex. **Methods:** From August 2018 to November 2021, 65 PCOS patients diagnosed and treated in the department of gynecology in our hospital were selected as the research objects, and they were divided into polycystic ovary syndrome obesity group ($n=30$, body mass index 28 kg/m^2) and multiple Cystic ovarian syndrome non-obese group ($n=35$, body mass index $<28 \text{ kg/m}^2$). Detect and calculate the two groups of vitamin D, ferritin, sICAM-1, insulin resistance, glucose and lipid metabolism indicators and conduct correlation analysis. **Results:** There were no difference in serum T₄, TSH and PRL between the two groups ($P>0.05$). The serum luteinizing hormone in the obese group The levels of LH, FSH and T were higher than those in the non-obese group ($P<0.05$). The levels of serum ferritin and sICAM-1 in the obese group were higher than those in the non-obese group, and the serum vitamin D levels were lower than those in the non-obese group ($P<0.05$). Insulin resistance index (HOMA-IR), insulin level (FINS), TG, TC and LDL-C in obese group were higher than those in non-obese group, while high density lipoprotein cholesterol (HDL-C) was lower than those in non-obese group ($P<0.05$). In obese patients with polycystic ovary syndrome, Pearson analysis showed that serum vitamin D, ferritin, sICAM-1 were correlated with insulin resistance and glucolipid metabolism ($P<0.05$). **Conclusion:** The polycystic ovary syndrome obese patients and non-obese patients Serum vitamin D, ferritin, sICAM-1, insulin resistance, glucose and lipid metabolism index levels are different, and serum vitamin D, ferritin, sICAM-1 levels are correlated with insulin resistance and glucose and lipid metabolism indexes.

Key words: Polycystic ovary syndrome; Vitamin D; Ferritin; Soluble intercellular adhesion molecule-1; Insulin resistance; Glucose and lipid metabolism

Chinese Library Classification(CLC): R588.6; R711.75 **Document code:** A

Article ID:1673-6273(2022)12-2318-04

* 基金项目:陕西省教育厅 2020 年服务地方专项科学研究计划(20JC030)

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(收稿日期:2021-11-25 接受日期:2021-12-21)

前言

多囊卵巢综合征(Polycystic ovarian syndrome, PCOS)是一种排卵障碍性疾病,因患者代谢功能、生殖内分泌发生紊乱,进而引发该疾病,其在生育年龄女性中的发病率为5.0%左右^[1]。PCOS的临床特征以卵巢功能障碍为主,在临床上可表现为代偿性高胰岛素血症、胰岛素抵抗、停止排卵、不孕、稀发排卵等症状^[2]。PCOS可应谢紊乱而增加心血管疾病和2型糖尿病发生的风险,且常因排卵障碍而导致不孕,严重影响患者的生存质量^[3]。PCOS的发病机制尚不十分清楚,但有研究发现:PCOS的基本病理生理特征为高胰岛素血症与胰岛素抵抗^[4]。特别是PCOS患者与患者的体重指数存在相关性,体重指数越高的患者,代谢综合征发生率高。1,25-二羟维生素D₃维生素D的活性代谢产物之一,可与维生素D受体(Vitamin D receptor, VDR)结合,从而介导机体多个器官组织的生理功能^[5]。铁蛋白为机体的重要调节蛋白,可调节钙和磷的吸收,与患者的胰岛素抵抗、糖脂代谢也存在一定的相关性^[6]。细胞间粘附分子可促进机体内血管内皮炎症反应,并形成血栓,进而与PCOS发生发展息息相关。血清可溶性细胞间粘附分子-1(Soluble Inter-cellular Adhesion Molecule-1, sICAM-1)是机体的一个重要炎症

标志,其参与了多个疾病的发病过程,在改善内皮功能、调节代谢等方面具有重要作用^[7,8]。本文具体探讨了PCOS肥胖患者血清维生素D、铁蛋白水平、sICAM-1与胰岛素抵抗、糖脂代谢指标的相关,望为患者预后改善提供一定的基础。

1 资料与方法

1.1 研究对象

采用总结性研究方法,研究时间为2018年8月到2021年11月,选择在本院妇科诊治的PCOS患者65例作为研究对象,以体重指数为28 kg/m²为界限,分为PCOS肥胖组(n=30,体重指数 $\geq$ 28 kg/m²)和PCOS非肥胖组(n=35,体重指数<28 kg/m²)。

纳入标准:临床与检测资料完整;符合PCOS的诊断标准^[9];初发患者;患者知情同意本研究;本院伦理委员会批准了此次研究。

排除标准:合并其他卵巢疾病的患者;入院前3个月内服用过其他任何影响体内性激素、糖脂代谢的患者;妊娠与哺乳期妇女;合并肿瘤的患者;严重肝脏和肾脏疾病患者;患有其他病因的高雄激素血症;其他女性不孕患者;营养不良患者。

两组资料对比无差异($P>0.05$)。见表1。

表1 一般资料对比

Table 1 Comparison of general data

Groups	n	Age (years)	Age of menarche (year)	Years of education (years)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Fasting blood glucose (mmol/L)	Body mass index (kg/m ²)
Obese group	30	35.29 $\pm$ 2.49	12.20 $\pm$ 1.84	14.18 $\pm$ 2.10	128.32 $\pm$ 2.43	78.28 $\pm$ 5.15	5.76 $\pm$ 0.36	29.13 $\pm$ 1.09
Non-obese group	35	35.10 $\pm$ 3.19	12.44 $\pm$ 2.09	13.43 $\pm$ 1.98	128.16 $\pm$ 3.33	78.44 $\pm$ 5.00	5.78 $\pm$ 0.26	24.26 $\pm$ 2.76

1.2 血清样本采集

所有入选者在月经来潮的第2-5 d抽取空腹静脉血,离心后分离上层血清,并在-40℃冰箱进行保存。标本尽量避免反复冻融,尽量只在检测前解冻并混匀。

1.3 血清维生素D、铁蛋白水平、sICAM-1与胰岛素抵抗、糖脂代谢指标检测

采用全自动生化分析法检测血清维生素D、铁蛋白水平,检测设备为Roche Cobas全自动生化分析仪。采用酶联免疫法(武汉博士德公司)检测血清sICAM-1含量。计算胰岛素抵抗指数(Homeostasis model assessment insulin resistance index, HOMA-IR), $HOMA-IR = \text{空腹血糖 (Fasting blood glucose, FBG)} \times \text{胰岛素水平 (Fasting insulin, FINS)} / 22.5$ 。同时测定两组患者的血脂水平,包括甘油三酯(Triglycerides, TG)、总胆固醇(Total cholesterol, TC)、低密度脂蛋白胆固醇(Low Density Lipoprotein Cholesterol, LDL-C)、高密度脂蛋白胆固醇(HDL Cholesterol, HDL-C)水平。测定与记录所有患者的性激素相关指标,包括甲状腺素(Thyroxine, T₄)、促卵泡生成素(Follicle Stimulating Hormone, FSH)、睾酮(Testosterone, T)、促甲状腺激素(Thyroid Stimulating Hormone, TSH)、促黄体生成素(Luteinizing hormone, LH)、泌乳素(Prolactin, PRL)等。

1.4 统计方法

本次研究的统计软件为SPSS22.00,检验水准 $\alpha=0.05$, $P<0.05$ 为差异有统计学意义。计量资料以均数 $\pm$ 标准差表示,计数数据以n%表示,对比采用t检验与卡方分析,相关性分析采用Pearson分析。

2 结果

2.1 性激素指标对比

两组的血清T₄、TSH与PRL对比差异无统计学意义($P>0.05$),肥胖组的血清LH、FSH、T水平高于非肥胖组($P<0.05$)。见表2。

2.2 血清维生素D、铁蛋白、sICAM-1水平对比

肥胖组的血清铁蛋白、sICAM-1水平高于非肥胖组,血清维生素D水平低于非肥胖组($P<0.05$)。见表3。

2.3 胰岛素抵抗、糖脂代谢指标对比

肥胖组的HOMA-IR、FINS、TC、TG、LDL-C高于非肥胖组, HDL-C低于非肥胖组($P<0.05$)。见表4。

2.4 相关性分析

在PCOS肥胖患者中,Pearson分析显示血清维生素D、铁蛋白、sICAM-1与胰岛素抵抗、糖脂代谢指标都存在相关性($P<0.05$)。见表5。

表 2 两组血清性激素指标对比(均数±标准差)

Table 2 Comparison of serum sex hormone indexes between the two groups (mean ± standard deviation)

Groups	n	T4(μg/dl)	TSH(μIU/mL)	PRL(ng/mL)	LH(IU/mL)	FSH(IU/mL)	T(ng/mL)
Obese group	30	8.82±0.36	3.29±0.24	16.29±1.68	7.87±0.46*	6.92±0.25*	0.50±0.11*
Non-obese group	35	8.81±0.32	3.31±0.23	16.33±2.19	6.28±1.00	6.11±0.33	0.22±0.06

Note: Compared with the non-obese group, * $P<0.05$.

表 3 两组血清维生素 D、铁蛋白、sICAM-1 水平对比(均数±标准差)

Table 3 Comparison of serum levels of vitamin D, ferritin and sICAM-1 between the two groups (mean ± standard deviation)

Groups	n	Vitamin D(ng/mL)	Ferritin	sICAM-1
Obese group	30	11.83±2.18*	93.95±2.18*	553.19±43.10*
Non-obese group	35	15.87±2.12	55.87±5.15	431.48±33.17

Note: Compared with the non-obese group, * $P<0.05$.

表 4 两组胰岛素抵抗、糖脂代谢指标对比(均数±标准差)

Table 4 Comparison of insulin resistance and glucolipid metabolism indexes between the two groups (mean ± standard deviation)

Groups	n	HOMA-IR	FINS(μU/mL)	TC(mmol/L)	TG(mmol/L)	LDL-C(mmol/L)	HDL-C(mmol/L)
Obese group	30	8.82±0.33*	34.02±2.58*	4.87±0.24*	1.43±0.14*	2.65±0.13*	1.10±0.22*
Non-obese group	35	5.89±0.28	23.54±4.44	4.03±0.29	1.09±0.22	2.12±0.09	1.87±0.33

Note: Compared with the non-obese group, * $P<0.05$.

表 5 PCOS 肥胖患者血清维生素 D、铁蛋白、sICAM-1 与胰岛素抵抗、糖脂代谢指标的相关性(n=30)

Table 5 Correlation between serum vitamin D, ferritin, sICAM-1 and insulin resistance and glucolipid metabolism in PCOS obese patients (n=30)

Indexs	Vitamin D	Ferritin	sICAM-1
HOMA-IR	-0.573 [#]	0.666 [#]	0.587 [#]
FINS	-0.722 [#]	0.553 [#]	0.616 [#]
TC	-0.614 [#]	0.722 [#]	0.638 [#]
TG	-0.588 [#]	0.588 [#]	0.700 [#]
LDL-C	-0.601 [#]	0.618 [#]	0.661 [#]
HDL-C	0.598 [#]	-0.666 [#]	-0.570 [#]

Note: [#] $P<0.05$.

3 讨论

PCOS 是一种内分泌紊乱性疾病, 在育龄期女性较为常见, 同时也是一种糖代谢异常、生殖功能障碍高度关联的特殊性综合性疾病^[10]。当前 PCOS 的发病机制尚不明确, 研究认为 PCOS 与下丘脑、垂体、性腺轴功能失调、胰岛素抵抗等多种因素有关。PCOS 的基因研究涉及卵泡的发生与成熟、甾体生成、糖脂代谢的相关基因等多方面^[11,12]。本研究显示两组的血清 T4、TSH 与 PRL 对比差异无统计学意义, 肥胖组的血清 LH、FSH、T 水平高于非肥胖组; 肥胖组的 HOMA-IR、FINS、TC、TG、LDL-C 高于非肥胖组, HDL-C 低于非肥胖组, 表明 PCOS 肥胖患者多伴有性激素异常与胰岛素抵抗、糖脂代谢指标异常。该结果与 Zeng X 等人^[13]以及 Liang R 等人^[14]的研究具有一致性。从机制上分析, 当前 PCOS 与肥胖的发生率均呈显著升高趋势, 两者并发的比例也在逐年增加。约 60 % 的 PCOS 患者有不同程度的体重身高, 肥胖发生率升高达正常人群的 7 倍, 发病时间提前了近 30 年。作为多囊卵巢综合征肥胖的主要特征,

高胰岛素血症产生原因为机体通过高表达胰岛素, 以维持血糖水平正常; 但当胰岛素分泌过量后, 其靶器官对胰岛素的敏感性逐渐降低, 形成胰岛素抵抗。但常规性激素指标检测的特异性较低, 波动也较大, 很难反映多囊卵巢综合征肥胖患者的病情状况^[15,16]。

PCOS 的病理生理改变存在异质性, 主要表现为卵巢呈多囊样改变、排卵功能障碍、子宫内膜增生病变、雄激素过多、胰岛素抵抗等。还可表现为皮质及皮质下间质明显增厚, 卵巢体积增大、闭锁卵泡明显增多、卵巢门细胞增生等^[17]。本研究显示肥胖组的血清铁蛋白、sICAM-1 水平高于非肥胖组, 血清维生素 D 水平低于非肥胖组。该结果与 Menichini D 等人^[18]以及 Tiongco RE 等人^[19]的研究具有一致性。从机制上分析, PCOS 患者体内维生素 D 缺乏症发病率较高, 维生素 D 缺乏的 PCOS 患者也多伴有各种慢性疾病^[20]。特别是维生素 D 缺乏可能参与多囊卵巢综合征患者中胰岛素抵抗的发生与发展, 严重维生素 D 缺乏与胰岛素抵抗存在显著相关性。sICAM-1 主要是评价内皮细胞损伤的重要标志^[21]。sICAM-1 表达升高表明机体出

现血栓形成、血管收缩、血小板激活,从而触发斑块破裂,以致动脉粥样硬化的风险性增加,导致心血管疾病的发生。血清铁蛋白是反映机体营养状况的重要指标,可损伤血管内皮,促进动脉粥样硬化以及粥样斑块破裂^[20,21]。

PCOS 的发病原因目前尚未完全明确,涉及的理论包括基因多态性学说、慢性炎症反应学说、青春期饮食障碍学等^[22,23]。本研究 Pearson 分析显示:PCOS 肥胖患者的血清维生素 D、铁蛋白、sICAM-1 与胰岛素抵抗、糖脂代谢指标均存在相关性。该结果与 Javed Z 等人^[24]以及郭小芳等人^[25]的研究具有相似性。从机制上分析,PCOS 患者存在胰岛素抵抗,后者增高血糖,激活血小板激活。机体的高血糖可提高血小板对于二磷酸腺苷刺激的反应性,进而加速氧化,而氧化的 LDL-C 可损伤内皮细胞,刺激炎症因子释放,诱导内皮细胞表面粘附分子的表达^[26,27]。且 PCOS 患者多伴有血脂异常,将会加重血管内皮细胞损伤,导致血管内皮 ICAM-1 表达升高^[28]。维生素 D 刺激胰岛素受体,可调节胰岛细胞内和细胞外的钙含量,对胰岛素分泌产生有利作用并增加胰岛素利用率,还导致胰岛素抵抗相关的炎症反应增强。同时 PCOS 肥胖患者体内铁储备增加可能是胰岛素抵抗的结果,特别是铁过量与血清磷脂酰胆碱亚群水平变化存在相关性^[29,30]。本研究也存在一定的不足,研究对象的纳入细分不足,未纳入正常人群,且样本数量比较少,为此对于明确 PCOS 肥胖发生机制还存在缺陷,将在下一步研究中进行分析。

综上所述,PCOS 肥胖患者与非肥胖患者的血清维生素 D、铁蛋白、sICAM-1、胰岛素抵抗、糖脂代谢指标水平存在差异,血清维生素 D、铁蛋白、sICAM-1 水平与胰岛素抵抗、糖脂代谢指标存在相关性。

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