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矮小症儿童和青少年出生体重与血清尿酸的相关性

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摘　要

目的：探究矮小症儿童和青少年出生体重(BW)与血清尿酸(UA)之间的相关性。方法：选取2013年03月至2019年02月在济宁医学院附属医院内分泌科就诊的矮小症儿童和青少年共478人，以BW 2.5 kg为切点，将受试者分为低出生体重(LBW定义为出生体重 < 2.5 kg)组和正常出生体重(NBW定义为出生体重≥ 2.5 kg，且≤4.0 kg)组。收集其出生信息及住院资料，分析矮小症儿童和青少年BW与UA之间的相关性。结果：LBW组UA水平显著高于NBW组(P < 0.05)，高尿酸血症(HUA)组体重指数(BMI)、LBW (%)显著高于非HUA组(P < 0.05)，HUA组BW显著低于非HUA组(P < 0.05)，Logistic回归分析显示BW、BMI是HUA的独立危险因素。结论：在矮小症儿童和青少年中，较低的出生体重与HUA的发病风险密切相关。

关键词

矮小症，低出生体重，高尿酸血症

Associations between Birth Weight and Serum Uric Acid in Children with Short Stature

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Abstract

Objective: To explore the relationship between birth weight (BW) and serum uric acid (UA) in children and adolescents with short stature. Methods: A total of 478 children and adolescents with short stature who were admitted to Endocrinology Department of Affiliated Hospital of Jining Medical University from March 2013 to February 2019 were selected. The cut-off point was BW 2.5 kg. Subjects were divided into low birth weight (LBW defined as birth weight < 2.5 kg) group and normal birth weight (NBW defined as birth weight ≥ 2.5 kg, and ≤ 4.0 kg) group. Data of birth and hospitalization were collected to analyze the correlation between BW and UA in children and adolescents with short stature. Results: The UA level in LBW group was significantly higher than that in NBW group (P < 0.05), body mass index (BMI) and LBW (%) in hyperuricemia (HUA) group were significantly higher than those in non-HUA group (P < 0.05), and BW in HUA group was significantly lower than that in non-HUA group (P < 0.05). Logistic regression analysis showed that BW and BMI were independent risk factors for HUA. Conclusion: Lower birth weight is associated with the risk of HUA in children and adolescents with short stature.

Keywords

Short Stature, Low Birth Weight, High Uric Acid

1. 引言

矮小症作为内分泌科常见病，是指在类似生活环境下，个体身高低于同性别、年龄、种族的正常人群平均身高的 2 个标准差(−2SD)或者低于第 3 个百分位[1]。矮小身材者会影响到儿童及成人时期的生活质量[2]。UA 是嘌呤代谢的最终产物，其正常生理功能有维持血压、抗氧化、保护细胞内的 DNA、抗衰老等作用，正常范围的尿酸水平有益于人类健康[3]。其偏差可反映代谢紊乱。在矮小症儿童和青少年中，UA 与矮小儿童和青少年的心脏代谢指标密切相关[4] [5] [6]，且 HUA 患病率较高。HUA 是现代社会常见的代谢性疾病，我们应积极寻找降低血清尿酸的因素。

50 多年前，研究表明，LBW 婴儿的 UA 水平显著增加[7]。随后，关于 LBW 与 UA 之间相关性的数据不断积累。大量研究表明，较低的 BW 与较高的 UA 相关[8] [9] [10]。到目前为止，关于 BW 与 UA 间相关性的研究在矮小症儿童和青少年中还没有被详细阐述。因此，在本研究中，我们旨在探讨矮小症儿童和青少年 BW 水平与 UA 水平的相关性。

2. 研究人群和方法

2.1. 研究人群

选取 2013 年 03 月至 2019 年 02 月在济宁医学院附属医院内分泌科就诊的矮小症儿童和青少年共 478 人。其数据信息均来自 GDDSD 研究(山东省生长发育疾病：队列随访研究) [11]。纳入标准如下：符合矮

小症诊断标准[1]；排除标准包括：1) 没有完整的出生资料，包括出生体重(BA)及胎龄(GA)，且 GA 大于 42 周；2) 没有 UA 数据的受试者；3) 有慢性肝肾疾病、染色体异常、占位性病变等肿瘤病史者。最终，共有 478 名参与者(348 名男性和 130 名女性)最终纳入我们的研究，平均年龄为 9.9 ± 3.5 岁。根据不同的出生体重，研究对象被分为低出生体重(LBW 定义为出生体重 < 2.5 kg)组和正常出生体重(NBW 定义为出生体重 ≥ 2.5 kg，且 ≤ 4.0 kg)组。

2.2. 出生资料

所有参与者的出生信息均来自医院的医疗记录，包括性别、年龄、体重和 GA、BW。计算 LBW 的百分比。

2.3. 临床基本参数及代谢指标

基本参数

身高测量：研究对象取光足站立位姿势，使用同一批身高计量器材误差精确范围为 0.1 厘米。体重测量：研究对象取光足站立位姿势，身着轻便衣物，使用同一批电子秤，误差精确范围为 0.1 公斤。体重指数(body mass index, BMI)计算公式为体重(kg)/身高(m^2)。根据中国 0~18 岁儿童、青少年生长曲线为参照计算身高标准差积分(height standard deviation score, HT SDS) [12]，受试者取坐位休息 5 min 后，使用自动血压仪测量收缩压(SBP)和舒张压(DBP)。

生化指标

所有患儿均为清晨抽取空腹静脉血，使用生化自动分析仪(Cobas c702，罗氏，中国上海)检测肝肾功能，及血脂[总胆固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、高密度脂蛋白(high density lipoprotein, HDL)、低密度脂蛋白(low density lipoprotein, LDL)]和空腹血糖(fasting blood glu-cose, FBG)、肌酐(Cr)和 UA 等生化指标。HUA 定义为 UA ≥ 327 μmol/L [5]。

激素测定　患儿均进行左旋多巴生长激素激发试验和胰岛素低血糖生长激素激发试验进行 GH 评估，采用化学发光法测定 GH 浓度，并选择其在 0、30、60、90、120 min 测得最大值作为生长激素峰值(GH peak)。

2.4. 统计分析

采用 SPSS 26.0 统计学软件对数据进行分析，正态分布的变量以平均值 ± 标准差($\bar{x}$ ± S)表示，分类变量以百分比(n, %)表示。偏态分布的变量以四分位数范围的中位数($M(P_{25}, P_{75})$)表示。连续变量采用独立样本 t 检验，分类变量采用卡方检验，检验两组临床和代谢指标的差异。对 HUA 的自变量进行 logistic 回归分析。统计学差异以 P 值(双尾) < 0.05 来定义。

3. 结果

3.1. 研究对象的基线资料特征

所有受试者的临床和生化特征见表 1。共有 478 名参与者(348 名男性和 130 名女性)，平均年龄 9.9 ± 3.5 岁。平均 BW 为 3.1 ± 0.5 Kg。LBW 的比例为 6%。HUA 百分比为 16.0%。比较 LBW 组与 NBW 组的临床及代谢特征如表 2 所示。结果表明，LBW 组 UA 水平高于 NBW 组(P < 0.001)。两组间 GH peak、HUA(%)的差异有统计学意义(P < 0.05)。其他临床及代谢指标 BMI、SBP、DBP、TC、TG、HDL-c、LDL-c、FPG、Cr、ALT 在 LBW 组与 NBW 组间无统计学差异(P > 0.05)。

3.2. 基于 SUA 水平的各变量比较

如表 3 所示，根据 UA 水平将受试者分为 HUA 组和 non-HUA 组，并对两组各变量进行比较。在人

口统计学和生化指标方面，与非 HUA 组相比，HUA 组 LBW%显著提高($P < 0.05$)，BW 显著降低($P < 0.001$)。在临床及代谢指标方面，HUA 组 BMI 高于非 HUA 组($P < 0.05$)，而 SBP、DBP、TC、TG、HDL-c、LDL-c、FPG、Cr、ALT、GH peak、GA 在两组间无统计学差异($P > 0.05$)。

3.3. 对 HUA 的自变量进行 Logistic 回归分析

根据表 3 的结果，以 HUA 为因变量，以 BMI、BW 为自变量进行 Logistic 回归分析，如表 4 所示，Logistic 回归分析显示，体重、BMI 进入回归模型(BW, OR: 0.342, 95% CI for OR: 0.200~0.583, $P < 0.001$; 对于 BMI, OR: 1.124, 95% CI OR: 1.043~1.211, $P = 0.002$)。

Table 1. Basic characteristics of the subjects
表 1. 研究对象基本特征描述

Variables	All
Sex (Male, n, %)	348 (73%)
Height (cm)	124.1 ± 18.2
HT SDS	−2.62 ± 0.5
GA (week)	39.5 ± 1.7
BW (kg)	3.1 ± 0.5
Age (years)	9.9 ± 3.5
BMI (kg/m^2)	16.7 ± 3.0
SBP (mmHg)	104.3 ± 12.1
DBP (mmHg)	62.1 ± 9
TC (mmol/L)	3.8 ± 0.7
TG (mmol/L)[a]	0.65 (0.51~0.87)
HDL-c (mmol/L)	1.4 ± 0.3
LDL-c (mmol/L)	2.1 ± 0.6
FPG (mmol/L)	4.7 ± 0.6
Cr (μmol/L)	40.6 ± 14.3
UA (μmol/L)	260 ± 71
ALT (U/L)	15.8 ± 8.7
GH peak (ng/mL)	7.2 (4.44~11.15)
LBW (%)	30 (6%)
HUA (%)	76 (16.0%)

HT SDS: the standard deviation score of height; GA: gestational age; BW: birth weight; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; FPG: fasting plasma glucose; Cr: Creatinine; UA: uric acid; ALT: alanine aminotransferase; GH: growth hormone; LBW: low birth weight.

Table 2. Clinical and metabolic characteristics between different groups
表 2. 不同组间临床和代谢指标的比较

Variables	NBW (n = 448)	LBW (n = 30)	P
Age (years)	9.9 ± 3.5	8.9 ± 3.7	0.129
BMI (kg/m^2)	16.7 ± 2.9	16.6 ± 4.3	0.907

Continued

SBP (mmHg)	104.5 ± 11.9	101.2 ± 14.6	0.148
DBP (mmHg)	62.2 ± 9.1	60.5 ± 7.8	0.324
TC (mmol/L)	3.8 ± 0.7	3.9 ± 0.7	0.815
TG (mmol/L) [a]	0.66 (0.51~0.89)	0.59 (0.44~0.76)	0.747
HDL-c (mmol/L)	1.4 ± 0.4	1.4 ± 0.3	0.857
LDL-c (mmol/L)	2.1 ± 0.6	2.2 ± 0.5	0.499
FPG (mmol/L)	4.7 ± 0.6	4.7 ± 0.7	0.761
Cr (μmol/L)	40.8 ± 14.5	38.3 ± 9.9	0.361
UA (μmol/L)	256.6 ± 69.5	308.6 ± 76.1	<0.001
ALT (U/L)	15.7 ± 8.6	16.5 ± 10.3	0.642
GH peak (ng/mL)	7.1 (4.4~10.9)	10.2 (5.7~16.9)	0.023
HUA (%)	15%	37%	0.003

Table 3. Metabolic characteristics between different groups
表 3. 不同组间代谢指标的比较

Variables	Non-HUA (n = 402)	HUA (n = 76)	P
Male (%)	289 (72%)	59 (78%)	0.373
Age (years)	9.7 ± 3.4	10.6 ± 3.9	0.085
BMI (kg/m^2)	16.5 ± 2.7	17.7 ± 3.9	0.010
SBP (mmHg)	103.9 ± 11.6	106.5 ± 14.3	0.149
DBP (mmHg)	62.2 ± 9	61.8 ± 9.2	0.773
TC (mmol/L)	3.90 ± 0.7	3.8 ± 0.7	0.270
TG (mmol/L) [a]	0.64 (0.51~0.86)	0.72 (0.5~0.96)	0.710
HDL-c (mmol/L)	1.4 ± 0.4	1.3 ± 0.3	0.054
LDL-c (mmol/L)	2.1 ± 0.6	2.1 ± 0.6	0.92
FPG (mmol/L)	4.7 ± 0.6	4.7 ± 0.6	0.325
Cr (μmol/L)	40.1 ± 14.9	43.2 ± 10.5	0.088
UA (μmol/L)	237.8 ± 49.5	376.4 ± 50.6	<0.001
ALT (U/L) [a]	15.5 ± 8.6	17.1 ± 8.9	0.138
GH peak (ng/mL)	7.0 (4.5~10.6)	9.8 (4.2~12.6)	0.142
GA (week)	39.5 ± 1.6	39.2 ± 2.2	0.155
BW (kg)	3.1 ± 0.4	2.9 ± 0.5	<0.001
LBW (%)	19 (4.7%)	11 (14.5%)	0.003

Table 4. The correlation between BW with HUA by logistic regression model
表 4. 用 logistic 回归模型分析 BW 与 HUA 的相关性

Variables	B	SE	P	OR	95% CI for OR
BW	−1.073	0.273	0.000	0.342	0.200~0.583
BMI	0.117	0.038	0.002	1.124	1.043~1.211

4. 讨论

本项研究对矮小症儿童和青少年人群进行横断面分析，分组研究显示LBW组UA水平显著高于NBW组，Logistic回归分析显示BW、BMI是HUA的独立危险因素。

据报道，近年来儿童和青少年的高尿酸血症比例有所增加。在我们的研究中，矮小症儿童和青少年高尿酸血症的比例高达16%，造成矮小症儿童和青少年高尿酸血症的原因暂不清楚，我们推断与挑食、偏食和过量摄入高糖饮料有关，这可能导致尿酸水平升高。较低的BW与较高的UA水平密切相关[13] [14]。这与Erika T. Rhone等[15]研究结果一致。Erika T. Rhone等对5390名12~15岁的美国青少年人群进行横断面研究，结果显示较低的出生体重与较高的血清尿酸相关。这种关系与肾小球滤过率(GFR)的变化无关，并且在血压正常和血压升高的患者中都存在。同时，血清尿酸水平是一种氧化应激标志物，在某些条件下可能会增加，这为缺氧奠定了基础。一项针对143名孕妇产后随访的研究表明[16]，LBW婴儿的母亲UA水平明显高于NBW婴儿的母亲，尿酸水平可作为孕期诊断为胎龄小的孕妇密切监测的预后参数。血尿酸升高被认为代谢综合征、血脂代谢紊乱的危险因素[17] [18]。越来越多的证据支持低出生体重和儿童和成人心脏代谢风险之间密切相关[19] [20] [21] [22]。我们的研究表明，BMI与UA水平呈正相关。与Goli [23]等研究结果一致。有研究认为BMI增高会增加胰岛素抵抗，HUA可能与胰岛素抵抗相关。

本研究存在一定的局限性。首先，本研究是横断面研究，无法确定因果关系。因此，本研究结果适用于中国矮小症儿童和青少年。在其他人群中可能发现不同的结果。此外，影响UA水平的因素很多，我们没有收集到有关UA的其他潜在混杂因素的数据。

5. 结论

我们发现了在矮小症儿童和青少年中，较低的出生体重与HUA的发病风险密切相关。UA水平与人类代谢密切相关，因此，在矮小症患者的诊疗工作中必须重视UA水平检测。

6. 声明

该研究由济宁医学院附属医院人类伦理委员会批准并获得患者父母的书面知情同意。

参考文献

[1] 沈永年, 王慕逖. 矮身材儿童诊治指南[J]. 中华儿科杂志, 2008, 46(6): 428-430.

[2] Backeljauw, P., Cappa, M., Kiess, W., *et al*. (2021) Impact of Short Stature on Quality of Life: A Systematic Literature Review. *Growth Hormone & IGF Research*, **57-58**, Article ID: 101392. https://doi.org/10.1016/j.ghir.2021.101392

[3] 马晨, 杨如雪, 汲宝兰. 成人睡眠和尿酸的研究进展[J]. 临床医学进展, 2022, 12(10): 9273-9277. https://doi.org/10.12677/acm.2022.12101341

[4] Chu, Y., Zhao, Q., Zhang, M., Ban, B. and Tao, H. (2021) Association between Serum Uric Acid and Triglycerides in Chinese Children and Adolescents with Short Stature. *Lipids in Health and Disease*, **20**, Article No. 1. https://doi.org/10.1186/s12944-020-01429-x

[5] Kou, S., Zhang, M., Ji, B., *et al*. (2021) Association between Systolic Blood Pressure and Uric Acid in Chinese Children and Adolescents with Idiopathic Short Stature: A Cross-Sectional Study. *Journal of Human Hypertension*, **35**, 472-478. https://doi.org/10.1038/s41371-020-0362-0

[6] Wang, P., Ji, B., Shao, Q., *et al*. (2018) Association between Insulin-Like Growth Factor-1 and Uric Acid in Chinese Children and Adolescents with Idiopathic Short Stature: A Cross-Sectional Study. *BioMed Research International*, **2018**, Article ID: 4259098. https://doi.org/10.1155/2018/4259098

[7] Marks, J.F., Kay, J., Baum, J. and Curry, L. (1968) Uric Acid Levels in Full-Term and Low-Birth-Weight Infants. *The Journal of Pediatrics*, **73**, 609-611. https://doi.org/10.1016/S0022-3476(68)80279-3

[8] Sipola-Leppänen, M., Vääräsmäki, M., Tikanmäki, M., *et al*. (2015) Cardiometabolic Risk Factors in Young Adults

Who Were Born Preterm. *The American Journal of Epidemiology*, **181**, 861-873. https://doi.org/10.1093/aje/kwu443

[9] Franco, M.C., Christofalo, D.M., Sawaya, A.L., *et al*. (2006) Effects of Low Birth Weight in 8- to 13-Year-Old Children: Implications in Endothelial Function and Uric Acid Levels. *Hypertension*, **48**, 45-50. https://doi.org/10.1161/01.HYP.0000223446.49596.3a

[10] Basioti, M., Giapros, V., Kostoula, A., *et al*. (2009) Growth Restriction at Birth and Kidney Function during Childhood. *American Journal of Kidney Diseases*, **54**, 850-858. https://doi.org/10.1053/j.ajkd.2009.05.017

[11] Zhao, Q., *et al*. (2021) A Retrospective Analysis of Patients with Short Stature in Eastern China between 2013 and 2019. *BioMed Research International*, **2021**, Article ID: 6640026. https://doi.org/10.1155/2021/6640026

[12] 李辉, 季成叶, 宗心南, 等. 中国 0-18 岁儿童、青少年身高、体重的标准化生长曲线[J]. 中华儿科杂志, 2009, 47(7): 487-492. https://doi.org/10.3760/cma.j.issn.0578-1310.2009.07.003

[13] Kaneshi, T., Yoshida, T., Ohshiro, T., *et al*. (2007) Birthweight and Risk Factors for Cardiovascular Diseases in Japanese Schoolchildren. *Pediatrics International*, **49**, 138-143. https://doi.org/10.1111/j.1442-200X.2007.02333.x

[14] Park, B., Park, E., Cho, S.J., *et al*. (2009) The Association between Fetal and Postnatal Growth Status and Serum Levels of Uric Acid in Children at 3 Years of Age. *American Journal of Hypertension*, **22**, 403-408. https://doi.org/10.1038/ajh.2009.12

[15] Rhone, E.T. and Carmody, J.B. (2017) Birthweight and Serum Uric Acid in American Adolescents. *Pediatrics International*, **59**, 948-950. https://doi.org/10.1111/ped.13328

[16] Sari, O., Akpak, Y.K., Yerebasmaz, N., *et al*. (2022) Evaluation of Obstructive Sleep Apnea Prevalence in Mothers of Infants with Low Birth Weight and Its Relationship with Serum Uric Acid Levels as a Hypoxia Marker. *The Journal of Maternal-Fetal & Neonatal Medicine*, **35**, 3525-3532. https://doi.org/10.1080/14767058.2020.1828332

[17] Zhang, S., Ma, Z., Li, Q., *et al*. (2020) Dose-Response Relationship between Distinct Serum Uric Acid Trajectories and Metabolic Syndrome Risk: A 5-Year Prospective Cohort Study. *Nutrition, Metabolism and Cardiovascular Diseases*, **31**, 1189-1199. https://doi.org/10.1016/j.numecd.2020.12.007

[18] Zeng, J., Lawrence, W.R., Yang, J., *et al*. (2021) Association between Serum Uric Acid and Obesity in Chinese Adults: A 9-Year Longitudinal Data Analysis. *BMJ Open*, **11**, e41919. https://doi.org/10.1136/bmjopen-2020-041919

[19] Huang, T., Wang, T., Zheng, Y., *et al*. (2019) Association of Birth Weight with Type 2 Diabetes and Glycemic Traits: A Mendelian Randomization Study. *JAMA Network Open*, **2**, e1910915.

[20] Bernhardsen, G.P., Stensrud, T., Hansen, B.H., *et al*. (2020) Birth Weight, Cardiometabolic Risk Factors and Effect Modification of Physical Activity in Children and Adolescents: Pooled Data from 12 International Studies. *International Journal of Obesity* (*London*), **44**, 2052-2063. https://doi.org/10.1038/s41366-020-0612-9

[21] Huang, X., Liu, J., Qi, L., *et al*. (2022) Birth Weight and the Risk of Cardiovascular Outcomes: A Report from the Large Population-Based UK Biobank Cohort Study. *Frontiers in Cardiovascular Medicine*, **9**, Article ID: 827491. https://doi.org/10.3389/fcvm.2022.827491

[22] Maguolo, A., Olivieri, F., Zusi, C., *et al*. (2021) The Risk of Metabolic Derangements Is Higher in Children and Adolescents with Overweight or Obesity Born Small for Gestational Age. *Nutrition, Metabolism and Cardiovascular Diseases*, **31**, 1903-1910. https://doi.org/10.1016/j.numecd.2021.02.025

[23] Goli, P., Riahi, R., Daniali, S.S., *et al*. (2020) Association of Serum Uric Acid Concentration with Components of Pediatric Metabolic Syndrome: A Systematic Review and Meta-Analysis. *Journal of Research in Medical Sciences*, **25**, 43. https://doi.org/10.4103/jrms.JRMS_733_19