

# 湖北省十堰市城区学龄前儿童尿金属水平与肥胖的关系

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## 摘要：

**[背景]** 金属暴露与成人肥胖有关，但缺乏关于学龄前儿童的研究证据。

**[目的]** 分析学龄前儿童尿金属水平与肥胖的关系。

**[方法]** 采用横断面设计，在湖北省十堰市城区抽取 1595 名学龄前儿童进行问卷调查和体格检查。根据世界卫生组织的相关标准，体质指数 (BMI)  $\geq$  同性别年龄第 95 百分位数 ( $P_{95}$ ) 为肥胖。采用电感耦合等离子体质谱法检测晨尿中 24 种金属浓度。根据尿金属浓度四分位数水平，将研究对象分为 Q1~Q4 组，用 LASSO 回归筛选多金属暴露模型中的变量，用二元 logistic 模型评估学龄前儿童单金属及多金属暴露水平与肥胖的关系。

**[结果]** 本研究最终纳入 1471 名儿童，平均年龄 (4.4 $\pm$ 1.0) 岁，男童占 55.6%。总肥胖率为 11.82%。在校正肥胖相关因素 (性别、年龄、出生体重等) 的单金属模型中，钒、铜、锰、铀 Q3 组儿童的肥胖患病风险分别是 Q1 组的 52%、56%、55%、75%，钼、钒、铷、铝、镉、砷、铀、铊 Q4 组儿童的肥胖患病风险分别是 Q1 组的 54%、56%、59%、52%、50%、39%、73%、55%；除铜、锰外，上述金属与儿童肥胖患病风险均具有线性趋势 (均  $P_{趋势} < 0.05$ )。通过 LASSO 回归筛选出 6 个金属钒、铝、镉、砷、铀、钛，共同构建多金属暴露模型。结果显示，砷 Q4 组对应的肥胖患病风险是 Q1 组的 50% (95% CI : 0.28~0.87)，并仍存在线性趋势 ( $P_{趋势} = 0.046$ )；铀 Q3 组对应的肥胖患病风险是 Q1 组的 53% (95% CI : 0.31~0.91)，但无线性趋势 ( $P_{趋势} = 0.131$ )。

**[结论]** 湖北省十堰市学龄前儿童部分尿金属水平与肥胖呈负相关，其中砷和铀可能是肥胖的重要影响因素。

**关键词：** 学龄前儿童；肥胖；尿；金属

**Association of urinary metals levels with obesity in urban preschoolers in Shiyan of Hubei Province** ZHU Meiqin<sup>1a, 1b</sup>, JI Hongxian<sup>2</sup>, YU Lili<sup>1b</sup>, LIU Yanli<sup>1a</sup>, LI Dong<sup>3</sup>, GAO Zuxiong<sup>1b</sup>, YANG Liting<sup>1b</sup>, ZHOU Shangcheng<sup>1a</sup>, LI Xiaowen<sup>3</sup>, DING Hongcheng<sup>3</sup>, WANG Jing<sup>1a, 1b, 3</sup> (1.a.School of Public Health and Health b.Center for Environment and Health in Water Source-to-North Diversion, Hubei University of Medicine, Shiyan, Hubei 442000, China; 2.Department of Child Health, Shiyan Maternal and Child Health Hospital, Shiyan, Hubei 442000, China; 3.Department of Endocrinology, Renmin Hospital, Hubei University of Medicine, Shiyan, Hubei 442000, China)

## Abstract:

**[Background]** Metal exposure is associated with obesity in adults, but evidence from studies on preschool children is insufficient.

**[Objective]** This study is designed to analyze the relationship between urinary metal levels and obesity in preschool children.

**[Methods]** In the cross-sectional study, a questionnaire survey and a physical examination were conducted among 1595 preschoolers in Shiyan of Hubei Province. According to the standards of the World Health Organization, body mass index (BMI)  $\geq$  the 95th ( $P_{95}$ ) percentile for their age and sex is considered to be obese. The urinary concentrations of 24 metals were determined by inductively coupled plasma mass spectrometry. The participants were divided into Q1 to Q4 groups according to the quartiles of urinary metal concentrations. The relationships between exposure levels to mono-metals and poly-metals and obesity in the preschoolers were evaluated

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by binary logistic models, and variables in the polymetallic exposure model were screened by Lasso regression.

**[Results]** A total of 1 471 children were included in this study, with a mean age of (4.4±1.0) years, and boys accounted for 55.6%. The overall obesity rate was 11.8%. In single-metal models that was adjusted for obesity-related factors (such as sex, age, birth weight), the risks of obesity for children in the vanadium, copper, manganese, and uranium Q3 groups were 52%, 56%, 55%, and 75% of those in the Q1 groups; the risks of obesity for children in the molybdenum, vanadium, rubidium, aluminum, cadmium, arsenic, uranium, and thallium Q4 groups were 54%, 56%, 59%, 52%, 50%, 39%, 73%, and 55% of those in the Q1 groups, respectively; except copper and manganese, above metals had a linear trend with the risk of childhood obesity ( $P_{\text{trend}} < 0.05$ ). Six metals such as vanadium, aluminum, cadmium, arsenic, uranium, and titanium selected by LASSO regression were included in the polymetallic exposure model, and the results showed that the risk of obesity for children in the arsenic Q4 group was 50% (95% CI: 0.28-0.87) of that in the Q1 group, and there was still a linear trend ( $P_{\text{trend}}=0.046$ ); the risk of obesity for children in the uranium Q3 group was 53% (95% CI: 0.31-0.91) of that in the Q1 group, but there was no linear trend ( $P_{\text{trend}}=0.131$ ).

**[Conclusion]** Some urinary metal levels are negatively correlated with obesity of preschool children in Shiyan city of Hubei province, among which arsenic and uranium may be potential critical influencing factors for obesity.

**Keywords:** preschool child; obesity; urine; metal

随着工业化进程的加速,越来越多的金属通过污染的土壤、空气、水、食物等途径进入人体<sup>[1]</sup>。中国儿童金属暴露水平较高:6~12岁儿童尿砷几何均数(geometric mean, GM)为11.4(10.7~12.1)  $\mu\text{g}\cdot\text{L}^{-1}$ <sup>[2]</sup>,超过美国成年人暴露水平<sup>[3]</sup>。金属具有内分泌干扰作用<sup>[4]</sup>,可以通过改变内源性激素的产生、释放、运输、代谢、结合,来扰乱内分泌系统的内环境平衡,影响正常的生长和发育,增加代谢性疾病的患病风险<sup>[5-6]</sup>。儿童处于生长发育的关键时期,是金属污染的敏感人群<sup>[7]</sup>。

在过去的几十年间儿童肥胖率快速增长<sup>[8]</sup>,除传统的饮食、运动等因素外,环境因素也会影响肥胖的发生<sup>[9-10]</sup>。研究发现金属暴露与成人肥胖有关<sup>[11]</sup>,但有关学龄前儿童金属暴露与肥胖相关的研究较少。Shao等<sup>[12]</sup>发现尿钡与6~19岁人群肥胖呈正相关,而尿镉、铅、钴则与之呈负相关。既往研究多基于铅、砷、镉等常见金属的单金属暴露<sup>[12-14]</sup>,缺乏对其他金属及多金属暴露的分析。因此本研究基于湖北省十堰市(中国南水北调水源地)学龄前城区儿童开展横断面研究,分别从单金属及多金属暴露的角度评估学龄前儿童23种尿金属水平与肥胖的关系。

## 1 对象与方法

### 1.1 研究对象

选取湖北省十堰市城区2019年3—6月参加妇幼保健院体检的7所幼儿园进行调查,共有1 595名2~6岁儿童,参与问卷调查的有1 492人,排除身高、体重、尿样缺失及问卷信息不全者最终纳入1 471名儿童。本研究经过湖北医药学院伦理审查委员会的批准(编号:2019-TH-80),儿童的监护人均签署知情同意书。

### 1.2 调查方法

采用自编流行病学问卷调查儿童及家庭成员的社会人口学特征和生活方式,包括儿童的性别、年龄、出生体重、母亲生产方式、挑食情况(挑食:经常或非常挑剔食物,对有的食物不感兴趣,吃得少或不吃)、是否吃蔬菜和肉(过去1周内是否食用过该食物)、运动、睡眠等;父母的身高、体重、文化水平、吸烟情况(吸烟:在过去6个月每天至少吸1根烟)、家庭收入等。调查员在调查前接受统一培训。由带班老师将问卷分发给家长,调查员在家长群进行讲解后,由家长填写。电话随访补充缺失信息。

### 1.3 尿金属的检测

家长用医用尿杯收集儿童空腹晨尿置于5 mL尿管交给调查员。尿液在2 h内运回实验室分装, -80°C保存,于2019年10月检测。检测前将尿液复温,震荡混匀后移取尿液200  $\mu\text{L}$ 到5 mL聚丙烯管中。加入40  $\mu\text{L}$ 的硝酸(Thermo Fisher, 美国),在4°C下消化过夜。次日在室温复温30 min,加入3.76 mL的稀释液[2.5 mL正丁醇(默克,德国)+超纯水稀释至500 mL]定容至4 mL,混匀、离心(3 000  $\text{r}\cdot\text{min}^{-1}$ ,  $r=20\text{ cm}$ , 10 min)。使用电感耦合等离子体质谱仪(Thermo Fisher, 美国)检测铍、钼、钒、铜、锰、铷、铝、砷、镉、铀、铊、钛、铬、铁、钴、镍、锌、硒、锶、锡、锑、钡、钨、铅24种尿金属。杨丽婷等<sup>[15]</sup>对尿金属检测的方法进行了详细描述。在质控过程中本实验使用了多元素储备液和内标液(Inorganic Ventures, 美国)、尿样质控(Sero, 挪威)和水样质控1640a(Gaithersburg MD, 美国)。质控样品在每测50个尿样后检测一次。金属加标回收率为73.4%~144.6%。金属检出限在0.000 02~0.134 57  $\mu\text{g}\cdot\text{L}^{-1}$ 之间。尿铍的未检出率大于50%,因此不纳入分析,

其他金属未检出率均小于2%。低于检出限的检测值,用检出限除以2代替。金属浓度均使用尿肌酐校正,肌酐采用肌酐试剂盒检测(南京建成生物,中国)。

#### 1.4 肥胖的定义

儿童穿轻薄衣服、脱鞋,采用医用电子秤(苏宏,中国)测量身高、体重,各保留一位小数,计算体质指数(body mass index, BMI), BMI=体重/身高<sup>2</sup>(kg·m<sup>-2</sup>)。根据世界卫生组织的相关标准,学龄前儿童BMI≥同性别、同年龄第95百分位数(P<sub>95</sub>)为肥胖<sup>[16]</sup>。

#### 1.5 统计学分析

采用EpiData3.1建立数据库,使用SPSS 22.0、R 4.0进行数据分析。连续性数据使用Kolmogorov-Smirnov进行正态性检验,正态分布数据用 $\bar{x}\pm s$ 表示,组间均值比较采用t检验。非正态分布数据用中位数及上下四分位数表示,采用非参数Mann-Whitney U检验进行组间比较。分类变量用频数和构成比表示, $\chi^2$ 检验进行组间比较。尿肌酐校正后的金属浓度呈偏态分布,进行log对数转换。采用Spearman相关系数,构建金属间的相关性热图。采用二元logistic回

归分析单金属暴露与肥胖的关系,并校正性别、年龄、出生体重等因素。采用LASSO回归,用10倍交叉验证法,基于 $\lambda$ 的最小均方误差<sup>[17]</sup>筛选与肥胖相关的变量,共同纳入logistic回归。双侧检验,检验水准 $\alpha=0.05$ 。

## 2 结果

### 2.1 研究人群的基本特征

本研究最终纳入1471名儿童,平均年龄为(4.4±1.0)岁,男童占55.6%。学龄前儿童总肥胖率为11.82%,其中男童为14.67%、女童为8.27%。不同性别、年龄、母亲生产方式、挑食情况的儿童之间肥胖率差异有统计学意义(均 $P<0.05$ )。与非肥胖儿童相比,肥胖儿童出生体重更重,父母的BMI更大,吃饭和睡觉时长更短(均 $P<0.05$ )。见表1。

### 2.2 尿金属水平

表2为学龄前儿童23种尿金属校正前后的浓度。经校正肌酐后,几何均数最大和最小的金属为铷和铀,分别为4580.35、0.05 $\mu\text{g}\cdot\text{g}^{-1}$ 。

表1 研究对象基本特征

Table 1 Baseline characteristics of study participants

变量 Variable	合计 Total (n=1471)	非肥胖儿童 Non-obese children (n=1297)	肥胖儿童 Obese children (n=174)	P
性别 (Sex) [n (%)]				<0.001
男 (Boy)	818 (55.6)	698 (53.8)	120 (69.0)	
女 (Girl)	653 (44.4)	599 (46.2)	54 (31.0)	
年龄 / 岁 (Age/year) ( $\bar{x}\pm s$ )	4.4±1.0	4.4±1.0	4.8±1.0	<0.001
BMI/ (kg·m <sup>-2</sup> ) ( $\bar{x}\pm s$ )	16.8±1.7	15.9±1.1	19.5±1.9	<0.001
出生体重/kg (Birth weight/kg) [M (P <sub>25</sub> , P <sub>75</sub> )]	3.3 (3.1, 3.6)	3.3 (3.0, 3.6)	3.4 (3.2, 3.7)	<0.001
父亲 BMI/ (kg·m <sup>-2</sup> ) [Father's BMI/ (kg·m <sup>-2</sup> )] [M (P <sub>25</sub> , P <sub>75</sub> )]	23.9 (22.0, 25.8)	23.7 (21.7, 25.7)	24.8 (23.2, 26.7)	<0.001
母亲 BMI/ (kg·m <sup>-2</sup> ) [Mother's BMI/ (kg·m <sup>-2</sup> )] [M (P <sub>25</sub> , P <sub>75</sub> )]	21.1 (19.7, 22.9)	21.0 (19.6, 22.8)	21.9 (20.4, 23.6)	<0.001
母亲生产方式 (Mother's mode of delivery) [n (%)]				<0.001
自然分娩 (Natural birth)	539 (36.6)	497 (38.3)	42 (24.1)	
剖宫产 (Cesarean section)	932 (63.4)	800 (61.7)	132 (75.9)	
喂养方式 (Feeding method) [n (%)]				0.62
母乳 (Breast milk)	837 (56.9)	732 (56.4)	105 (60.3)	
混合 (Mixing)	502 (34.1)	447 (34.5)	55 (31.6)	
人工 (Artificial)	132 (9.0)	118 (9.1)	14 (8.1)	
独生子女 (Only-child) [n (%)]				0.42
否 (No)	660 (44.9)	577 (44.5)	83 (47.7)	
是 (Yes)	811 (55.1)	720 (55.5)	91 (52.3)	
父亲的文化程度 (Father's education level) [n (%)]				0.48
初中及以下 (Junior high school and below)	149 (10.1)	134 (10.3)	15 (8.6)	
高中及中专 (High school and junior college)	513 (34.9)	457 (35.2)	56 (32.2)	
大学及以上 (University and above)	809 (55.0)	706 (54.5)	103 (59.2)	
母亲的文化程度 (Mother's education level) [n (%)]				0.30
初中及以下 (Junior high school and below)	43 (2.9)	41 (3.2)	2 (1.2)	
高中及中专 (High school and junior college)	869 (59.1)	767 (59.1)	102 (58.6)	
大学及以上 (University and above)	559 (38.0)	489 (37.7)	70 (40.2)	

表 1 续

变量 Variable	合计 Total (n=1471)	非肥胖儿童 Non-obese children (n=1297)	肥胖儿童 Obese children (n=174)	P
父母吸烟 (Parental smoking) [n (%)]				0.42
否 (No)	1175 (79.9)	1040 (80.2)	135 (77.6)	
是 (Yes)	296 (20.1)	257 (19.8)	39 (22.4)	
每天电子产品使用时长/min (Screen time every day/min) [M (P <sub>25</sub> , P <sub>75</sub> )]	60 (30, 90)	60 (30, 80)	60 (30, 90)	0.37
每天睡觉时长/h (Sleep duration every day/h) [M (P <sub>25</sub> , P <sub>75</sub> )]	9.8 (9.5, 10)	9.8 (9.5, 10)	9.5 (9.2, 10)	<b>0.001</b>
每餐吃饭时长/min (Meal duration every meal/min) [M (P <sub>25</sub> , P <sub>75</sub> )]	20 (20, 30)	20 (20, 30)	20 (15, 25)	<b>&lt;0.001</b>
家庭人均月收入/元 (Household monthly income per capita/yuan) [n (%)]				0.07
≤ 4999	929 (63.1)	819 (63.1)	110 (63.2)	
5000~11999	453 (30.8)	406 (31.3)	47 (27.0)	
≥ 12000	89 (6.1)	72 (5.6)	17 (9.8)	
每天运动时间/h (Physical activities every day/h) [n (%)]				0.60
<2	989 (67.2)	869 (67.0)	120 (69.0)	
≥2	482 (32.8)	428 (33.0)	54 (31.0)	
吃蔬菜 (Eat vegetables) [n (%)]				0.52
否 (No)	795 (54.0)	697 (53.7)	98 (56.3)	
是 (Yes)	676 (46.0)	600 (46.3)	76 (43.7)	
吃肉 (Eat meat) [n (%)]				0.26 <sup>a</sup>
否 (No)	49 (3.0)	46 (3.5)	3 (1.7)	
是 (Yes)	1422 (97.0)	1251 (96.5)	171 (98.3)	
挑食 (Picky eater) [n (%)]				<b>0.001</b>
否 (No)	423 (28.8)	355 (27.4)	68 (39.1)	
是 (Yes)	1048 (71.2)	942 (72.6)	106 (60.9)	

[注] BMI：体质指数。a：使用 Fisher's 精确检验。

[Note] BMI: Body mass index. a: Fisher's exact test.

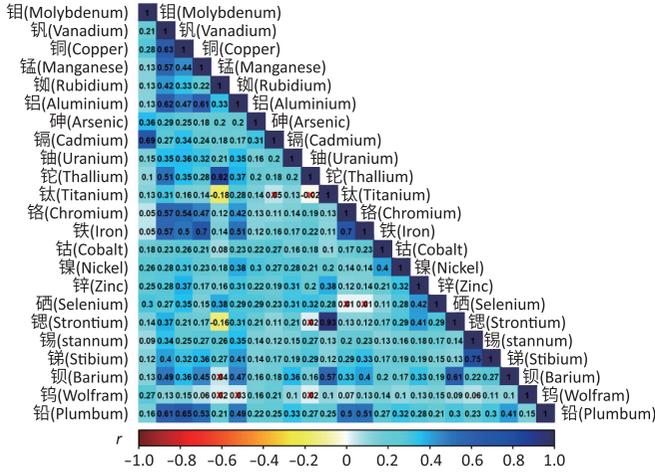
表 2 研究对象的校正前后尿金属浓度

Table 2 Crude and creatinine-adjusted urinary metal concentrations in study participants

金属 Metal	未校正肌酐的尿金属质量浓度 / (μg·L <sup>-1</sup> ) Crude urinary metal concentrations / (μg·L <sup>-1</sup> )						校正肌酐的尿金属质量分数 / (μg·g <sup>-1</sup> ) Creatinine-adjusted urinary metal concentrations / (μg·g <sup>-1</sup> )					
	几何均数 Geometric mean	P <sub>5</sub>	P <sub>25</sub>	P <sub>50</sub>	P <sub>75</sub>	P <sub>95</sub>	几何均数 Geometric mean	P <sub>5</sub>	P <sub>25</sub>	P <sub>50</sub>	P <sub>75</sub>	P <sub>95</sub>
钼 (Molybdenum)	78.19	23.06	49.84	78.47	125.65	257.75	366.23	130.03	256.88	368.37	529.02	1078.12
钒 (Vanadium)	0.32	0.17	0.24	0.31	0.41	0.69	1.50	0.64	1.03	1.45	2.09	4.07
铜 (Copper)	15.20	6.47	10.70	14.93	21.67	39.21	71.20	34.88	52.28	65.23	92.22	192.29
锰 (Manganese)	0.62	0.14	0.40	0.62	1.04	2.98	2.89	0.59	1.59	2.94	5.67	17.56
铷 (Rubidium)	977.93	400.47	669.93	983.45	1401.72	2791.70	4580.35	1931.48	3218.03	4574.21	6494.61	12480.57
铝 (Aluminium)	27.16	14.95	21.02	26.52	33.65	53.83	127.21	51.08	82.46	122.14	183.68	372.37
砷 (Arsenic)	23.23	8.28	15.11	23.20	35.60	69.12	108.83	45.31	80.63	107.76	147.37	296.74
镉 (Cadmium)	0.17	0.06	0.11	0.17	0.26	0.49	0.79	0.36	0.58	0.79	1.08	1.84
铀 (Uranium)	0.05	0.00	0.01	0.01	0.02	0.04	0.05	0.02	0.03	0.05	0.08	0.19
铊 (Thallium)	0.18	0.07	0.12	0.18	0.26	0.44	0.83	0.34	0.57	0.83	1.23	2.25
钛 (Titanium)	80.41	16.50	46.66	89.41	158.51	297.70	376.62	68.85	219.68	420.86	728.94	1366.35
铬 (Chromium)	0.74	0.16	0.37	0.65	1.51	4.42	3.45	0.70	1.59	2.98	6.97	24.84
铁 (Iron)	20.76	4.87	10.34	17.59	37.00	148.09	97.24	20.50	45.87	83.21	184.36	807.23
钴 (Cobalt)	0.29	0.09	0.18	0.29	0.47	1.02	1.37	0.53	0.90	1.32	2.02	4.17
镍 (Nickel)	4.22	1.65	2.80	4.08	6.18	12.02	19.77	8.35	13.87	19.23	27.68	52.60
锌 (Zinc)	459.28	178.94	325.29	466.44	681.41	1098.49	2151.11	1045.06	1697.00	2204.01	2841.80	4205.68
硒 (Selenium)	15.86	6.85	11.44	16.34	22.70	34.90	74.30	42.94	59.45	75.40	93.88	132.43
锶 (Strontium)	111.58	30.22	74.11	120.53	190.45	315.26	522.62	134.66	360.50	586.15	857.35	1394.58
锡 (Stannum)	4.95	0.66	3.33	5.66	8.99	18.87	23.18	2.87	14.34	25.32	44.08	100.17
锑 (Stibium)	0.26	0.07	0.12	0.18	0.26	0.44	1.27	0.34	0.57	0.83	1.23	2.25
钡 (Barium)	2.87	0.88	1.86	2.94	4.53	9.49	13.42	3.60	8.20	13.47	22.51	49.94
钨 (Wolfram)	0.26	0.05	0.13	0.23	0.44	2.99	1.21	0.28	0.64	1.09	1.86	14.20
铅 (Plumbum)	0.97	0.35	0.60	0.92	1.50	3.08	4.55	1.75	2.76	4.10	6.73	17.91

### 2.3 尿金属浓度间的相关性

图1显示,经肌酐校正和log对数转换后的大多数金属浓度间呈正相关,铝、钒、锰、铁、铬、铜、铷、铈、镉、钼、钛、锶、钨间相关系数较大,在0.61~0.93之间(均 $P < 0.05$ )。



[注] 红色x表示 $P > 0.05$ 。

[Note] Red x indicates  $P > 0.05$ .

图1 尿金属浓度间的相关性

Figure 1 Correlation between urinary metal concentrations

### 2.4 学龄前儿童单金属暴露与肥胖风险的关系

将尿金属浓度按照四分位数分为Q1~Q4组。logistic回归分析结果显示,校正性别、年龄、出生体重等因素后,钒、铜、锰、铷Q3组儿童的肥胖患病风险分别是Q1组的52%、56%、55%、75%,钼、钒、铷、铝、镉、砷、铈、钨Q4组儿童的肥胖患病风险分别是Q1组的54%、56%、59%、52%、50%、39%、73%、55%。除铜、锰外,上述金属与儿童肥胖患病风险均具有线性趋势(均 $P_{趋势} < 0.05$ )。见表3。

### 2.5 学龄前儿童多金属暴露与肥胖风险的关系

在λ的最小均方误差处,往右选择了尿钒、铝、镉、砷、铷、钛这6个金属及儿童年龄、性别、出生体重、是否吃肉、是否挑食、吃饭时长、睡觉时长、父母BMI、母亲的生产方式、父亲的教育程度、家庭收入这12个与肥胖相关的变量,见补充材料图S1。

将LASSO回归筛选的6个金属同时纳入logistic回归模型,并校正其他12个因素。结果显示,砷Q4组对应的肥胖患病风险是Q1组的50% (95% CI : 0.28~0.87), 并仍存在线性趋势 ( $P_{趋势} = 0.046$ ) ; 铷Q3组对应的肥胖患病风险是Q1组的53% (95% CI : 0.31~0.91), 但无线性趋势 ( $P_{趋势} = 0.131$ ) ; 其他金属与肥胖患病风险无统计学意义 ( $P_{趋势} > 0.05$ )。见表4。

表3 学龄前儿童尿单金属暴露与肥胖关系的 logistic 回归分析  
Table 3 Logistic regression analysis of the relationship between urinary monometallic exposure and obesity in preschool children

金属 Metal	OR (95% CI)				$P_{趋势}$ $P_{trend}$
	Q1	Q2	Q3	Q4	
钼 Molybdenum	1.00 <sup>a</sup>	0.73 (0.47~1.12)	0.83 (0.55~1.27)	0.50 (0.31~0.81) *	<b>0.009</b>
	1.00 <sup>b</sup>	0.77 (0.49~1.21)	0.87 (0.56~1.36)	0.54 (0.33~0.89) *	<b>0.030</b>
钒 Vanadium	1.00 <sup>a</sup>	0.63 (0.42~0.97)	0.52 (0.33~0.81) *	0.52 (0.33~0.81) *	<b>0.002</b>
	1.00 <sup>b</sup>	0.64 (0.41~1.00)	0.52 (0.32~0.82) *	0.56 (0.35~0.89) *	<b>0.008</b>
铜 Copper	1.00 <sup>a</sup>	0.66 (0.43~1.00)	0.47 (0.30~0.74) *	0.55 (0.36~0.85) *	<b>0.001</b>
	1.00 <sup>b</sup>	0.82 (0.53~1.28)	0.56 (0.34~0.91) *	0.78 (0.49~1.24)	0.076
锰 Manganese	1.00 <sup>a</sup>	0.96 (0.63~1.44)	0.55 (0.35~0.88) *	0.63 (0.40~0.99) *	<b>0.011</b>
	1.00 <sup>b</sup>	0.91 (0.59~1.41)	0.55 (0.34~0.89) *	0.71 (0.44~1.14)	0.050
铷 Rubidium	1.00 <sup>a</sup>	0.65 (0.43~0.99)	0.51 (0.33~0.79) *	0.46 (0.29~0.72) *	<b>&lt;0.001</b>
	1.00 <sup>b</sup>	0.75 (0.48~1.16)	0.63 (0.40~1.01)	0.59 (0.37~0.96) *	<b>0.023</b>
铝 Aluminium	1.00 <sup>a</sup>	0.58 (0.38~0.88)	0.61 (0.40~0.93) *	0.39 (0.24~0.62) *	<b>&lt;0.001</b>
	1.00 <sup>b</sup>	0.63 (0.40~0.98)	0.74 (0.48~1.16)	0.52 (0.31~0.86) *	<b>0.017</b>
镉 Cadmium	1.00 <sup>a</sup>	0.62 (0.40~0.96)	0.69 (0.45~1.06)	0.52 (0.33~0.81) *	<b>0.007</b>
	1.00 <sup>b</sup>	0.60 (0.38~0.95)	0.64 (0.41~1.01)	0.50 (0.31~0.80) *	<b>0.005</b>
砷 Arsenic	1.00 <sup>a</sup>	0.57 (0.37~0.88)	0.92 (0.62~1.38)	0.37 (0.22~0.60) *	<b>0.001</b>
	1.00 <sup>b</sup>	0.53 (0.34~0.85)	0.94 (0.61~1.43)	0.39 (0.23~0.65) *	<b>0.003</b>
铷 Uranium	1.00 <sup>a</sup>	0.77 (0.51~1.15)	0.38 (0.24~0.62) *	0.58 (0.37~0.89) *	<b>0.002</b>
	1.00 <sup>b</sup>	0.77 (0.50~1.19)	0.75 (0.26~0.72) *	0.73 (0.39~0.98) *	<b>0.012</b>
铈 Thallium	1.00 <sup>a</sup>	0.58 (0.38~0.88)	0.57 (0.37~0.88) *	0.48 (0.31~0.75) *	<b>0.001</b>
	1.00 <sup>b</sup>	0.66 (0.42~1.03)	0.64 (0.41~1.01)	0.55 (0.34~0.88) *	<b>0.011</b>
钛 Titanium	1.00 <sup>a</sup>	1.08 (0.69~1.70)	1.03 (0.65~1.63)	1.17 (0.75~1.83)	0.562
	1.00 <sup>b</sup>	1.09 (0.68~1.75)	0.98 (0.61~1.58)	1.20 (0.75~1.92)	0.558
铬 Chromium	1.00 <sup>a</sup>	1.02 (0.66~1.58)	1.08 (0.70~1.66)	0.75 (0.47~1.20)	0.244
	1.00 <sup>b</sup>	1.10 (0.69~1.75)	1.10 (0.69~1.74)	0.87 (0.53~1.43)	0.565
铁 Iron	1.00 <sup>a</sup>	1.28 (0.84~1.95)	0.74 (0.46~1.18)	0.76 (0.48~1.21)	0.073
	1.00 <sup>b</sup>	1.39 (0.89~2.16)	0.81 (0.50~1.32)	0.90 (0.55~1.46)	0.300
钴 Cobalt	1.00 <sup>a</sup>	0.88 (0.57~1.37)	0.86 (0.56~1.33)	0.75 (0.48~1.18)	0.221
	1.00 <sup>b</sup>	0.91 (0.58~1.45)	0.92 (0.58~1.45)	0.83 (0.52~1.32)	0.446
镍 Nickel	1.00 <sup>a</sup>	0.69 (0.44~1.07)	0.75 (0.49~1.15)	0.69 (0.45~1.07)	0.137
	1.00 <sup>b</sup>	0.69 (0.44~1.10)	0.81 (0.52~1.28)	0.81 (0.51~1.28)	0.473
锌 Zinc	1.00 <sup>a</sup>	1.11 (0.72~1.72)	1.10 (0.71~1.71)	0.75 (0.47~1.21)	0.273
	1.00 <sup>b</sup>	1.12 (0.70~1.77)	1.26 (0.79~1.99)	0.94 (0.57~1.56)	0.992
硒 Selenium	1.00 <sup>a</sup>	0.89 (0.59~1.35)	0.62 (0.39~0.96)	0.56 (0.35~0.89)	<b>0.005</b>
	1.00 <sup>b</sup>	1.02 (0.66~1.58)	0.67 (0.42~1.07)	0.76 (0.47~1.25)	0.135
锶 Strontium	1.00 <sup>a</sup>	1.22 (0.78~1.91)	1.00 (0.63~1.59)	1.17 (0.75~1.84)	0.657
	1.00 <sup>b</sup>	1.21 (0.75~1.93)	1.03 (0.63~1.67)	1.12 (0.70~1.79)	0.769
锡 Stannum	1.00 <sup>a</sup>	1.02 (0.67~1.55)	0.73 (0.47~1.15)	0.59 (0.37~0.94)	<b>0.017</b>
	1.00 <sup>b</sup>	1.39 (0.89~2.16)	0.81 (0.50~1.32)	0.90 (0.55~1.46)	0.161

续表 3

金属 Metal	OR (95%CI)				P <sub>趋势</sub> P <sub>trend</sub>
	Q1	Q2	Q3	Q4	
锑 Stibium	1.00 <sup>a</sup>	0.79 (0.52~1.21)	0.68 (0.44~1.05)	0.53 (0.33~0.84)	<b>0.005</b>
	1.00 <sup>b</sup>	0.78 (0.50~1.21)	0.81 (0.51~1.27)	0.66 (0.41~1.07)	0.105
钡 Barium	1.00 <sup>a</sup>	0.74 (0.48~1.13)	0.63 (0.40~0.97)	0.64 (0.41~1.00)	<b>0.032</b>
	1.00 <sup>b</sup>	0.83 (0.53~1.30)	0.71 (0.45~1.13)	0.73 (0.46~1.16)	0.113
钨 Wolfram	1.00 <sup>a</sup>	1.20 (0.79~1.84)	0.87 (0.55~1.37)	0.78 (0.49~1.24)	0.154
	1.00 <sup>b</sup>	1.29 (0.82~2.03)	1.02 (0.63~1.63)	0.83 (0.51~1.35)	0.308
铅 Plumbum	1.00 <sup>a</sup>	1.04 (0.68~1.59)	0.77 (0.49~1.21)	0.68 (0.43~1.08)	0.053
	1.00 <sup>b</sup>	1.05 (0.67~1.63)	0.75 (0.47~1.20)	0.73 (0.45~1.19)	0.110

[注] \* : P<0.05 ; a : 未校正其他因素 ; b : 将每个尿金属单个纳入并校正儿童性别、年龄、出生体重、睡觉时长、吃饭时长、是否挑食, 父母 BMI、母亲生产方式。金属浓度经尿肌酐校正并经 log 对数转化。

[Note] \* : P<0.05; a: Crude model; b: Each urinary metal is individually included and corrected for child's sex, age, birth weight, sleep duration, meal duration, picky eater, parental BMI, and maternal mode of delivery. Urinary metal concentrations are corrected for urinary creatinine and converted using the natural logarithm.

表 4 学龄前儿童尿多金属暴露与肥胖关系的 logistic 回归分析  
Table 4 Logistic regression analysis on the relationship between urinary polymetallic exposure and obesity in preschool children

金属 Metal	OR (95%CI)				P <sub>趋势</sub> P <sub>trend</sub>
	Q1	Q2	Q3	Q4	
钒 Vanadium	1.00 <sup>a</sup>	0.82 (0.52~1.30)	0.76 (0.45~1.27)	0.87 (0.49~1.55)	0.613
	1.00 <sup>b</sup>	0.77 (0.48~1.25)	0.67 (0.39~1.15)	0.81 (0.44~1.48)	0.404
铝 Aluminium	1.00 <sup>a</sup>	0.61 (0.39~0.95)	0.72 (0.45~1.15)	0.47 (0.26~0.84) *	<b>0.020</b>
	1.00 <sup>b</sup>	0.68 (0.43~1.10)	0.92 (0.56~1.53)	0.68 (0.36~1.27)	0.383
镉 Cadmium	1.00 <sup>a</sup>	0.71 (0.45~1.12)	0.85 (0.54~1.35)	0.67 (0.41~1.11)	0.217
	1.00 <sup>b</sup>	0.63 (0.39~1.03)	0.78 (0.48~1.28)	0.64 (0.38~1.09)	0.146
砷 Arsenic	1.00 <sup>a</sup>	0.65 (0.41~1.04)	1.14 (0.74~1.76)	0.49 (0.29~0.84) *	<b>0.027</b>
	1.00 <sup>b</sup>	0.59 (0.36~0.97) *	1.13 (0.71~1.80)	0.50 (0.28~0.87) *	<b>0.046</b>
铀 Uranium	1.00 <sup>a</sup>	0.86 (0.56~1.32)	0.51 (0.31~0.84) *	0.85 (0.53~1.36)	0.127
	1.00 <sup>b</sup>	0.80 (0.51~1.26)	0.53 (0.31~0.91) *	0.81 (0.48~1.34)	0.131
钛 Titanium	1.00 <sup>a</sup>	1.31 (0.82~2.10)	1.29 (0.80~2.09)	1.70 (1.05~2.77)	0.055
	1.00 <sup>b</sup>	1.31 (0.80~2.16)	1.18 (0.71~1.96)	1.62 (0.96~2.72)	0.146

[注] 多金属模型: 由钒、铝、镉、砷、铀、钛 6 种金属共同构建的模型; \* : P<0.05 ; a : 未进行其他因素校正 ; b : 模型校正了儿童年龄、性别、出生体重、是否吃肉、挑食、吃饭速度、睡觉时长, 父母 BMI、母亲生产方式、父亲的教育程度、家庭收入。金属浓度经尿肌酐校正并进行 log 自然对数转换。

[Note] Polymetallic model: A model constructed from 6 metals including vanadium, aluminum, cadmium, arsenic, uranium, and titanium; \* : P<0.05; a: Crude model; b: Each urinary metal is individually included and corrected for child's sex, age, birth weight, sleep duration, meal duration, eat meat, picky eater, parental BMI, maternal mode of delivery, father's education level, and household income. Urinary metal concentrations are corrected for urinary creatinine and converted using the natural logarithm.

### 3 讨论

本研究中学龄前儿童的肥胖率为 11.82%, 接近于王付曼等<sup>[18]</sup>调查的中国 7 个城市的学龄前儿童 12.4% 的肥胖率, 但高于杨可欣等<sup>[19]</sup>关于北京市学龄前儿童超重肥胖现状调查的结果 (8.21%)。

儿童肥胖可能与环境因素有关<sup>[10]</sup>, 本研究在单金属模型中发现多个尿金属与儿童肥胖呈负相关, 但目前有关金属暴露与儿童肥胖关系的研究较少, 且结果存在较大差异。Vrijheid 等<sup>[20]</sup>发现血清钼与 BMI-Z 评分呈负相关, 而本研究则发现尿钼与儿童肥胖呈负相关, 这与墨西哥一项出生队列研究发现的低尿钼与高 BMI-Z 评分的结果一致<sup>[21]</sup>。钼作为人体必需的微量元素, 对人体碳水化合物及脂肪的代谢具有重要作用。本研究和 Tascilar 等<sup>[22]</sup>均发现肥胖儿童的尿钼水平低于非肥胖儿童, Tinkov 等<sup>[23]</sup>的研究发现血清钼与 BMI 呈负相关, 前瞻性队列研究发现产前钼暴露会增加低出生体重儿的风险<sup>[24]</sup>。这些研究提示钼可能与 BMI 呈负相关。钼具有模拟胰岛素, 对抗胰岛素抵抗, 调节脂肪组织的内分泌功能及降低食欲生成信号的作用<sup>[25-27]</sup>。Vrijheid 等<sup>[20]</sup>和 Yang 等<sup>[28]</sup>发现儿童和成人的血清铜与 BMI 呈正相关。Fan 等<sup>[29]</sup>发现高血锰与儿童青少年肥胖呈正相关。但本研究观察到儿童尿铜、锰与儿童肥胖呈负相关。这种差异可能是由生物标记物的不同导致。钼是无毒微量元素, 目前还没有其他有关钼与肥胖相关性的研究, 未来需要进一步验证。

铝、镉、砷、铀为非必需微量元素。本研究观察到尿铝与学龄前儿童肥胖呈负相关。既往儿童铝暴露与肥胖关联的研究很少。Tinkov 等<sup>[30]</sup>发现肥胖成人尿铝水平比非肥胖成人更高。不同种族、不同年龄段人群对铝暴露的剂量及吸收率存在差异。Tietz 等<sup>[31]</sup>发现与其他年龄段相比, 3~6 岁儿童对食物中铝吸收量最高。本研究中的儿童尿铝质量浓度为 27.16 μg·L<sup>-1</sup>, Tinkov 等<sup>[30]</sup>研究发现成人中尿铝质量浓度为 19 μg·L<sup>-1</sup>, 但儿童尿铝浓度是否高于成人需要进一步研究。本研究有关儿童镉暴露与肥胖关系的结果与美国儿童青少年的横断面研究结果一致<sup>[12]</sup>。这一结果也在两项有关儿童镉暴露的队列中得到了验证<sup>[14, 32]</sup>。镉具有模拟激素和干扰内分泌的功能<sup>[33]</sup>, 可以模拟雄激素和雌激素的作用, 激活雌激素受体, 影响垂体分泌激素和孕激素的产生, 进而增加脂肪动员和脂肪分解<sup>[34-35]</sup>。Su 等<sup>[13]</sup>在中国台湾青少年中发现尿砷与 BMI 呈负相关, 本研究发现了类似结果, 这可能与砷具有提高血

清瘦素的水平,抑制脂肪细胞的合成有关<sup>[36]</sup>。砷在体内可以代谢为甲基化砷,本研究直接检测了总尿砷,因此需要在未来进一步检测、评估不同类型的体内砷代谢标志物与儿童肥胖风险的关系。Goodson等<sup>[37]</sup>检测了儿童唾液中N1-甲基-2-吡啶-5-羧酰胺(铀吸收的生物标记物),认为铀暴露可以增加科威特儿童肥胖患病风险,而本研究观察到尿铀与儿童肥胖呈负相关。这可能是导致研究结果存在差异的原因。

铊是一种具有潜在毒性的金属,既往铊暴露与儿童肥胖关联的研究较少。本研究发现铊与儿童肥胖呈负相关,关联的性质和机制还需要更多的人群研究及细胞动物实验来验证。

在多金属暴露中,只有尿砷和尿铀与儿童肥胖呈负相关。不同金属同时作用于人体时会产生联合、协同或抑制作用<sup>[11, 38]</sup>,砷和铀可能是肥胖的重要影响因素,但具体作用机制需要体内、体外研究来进一步探索。

本研究首次对中国南水北调水源地的儿童尿金属暴露水平与肥胖的关系进行了探索,采用LASSO回归进行多金属模型变量的筛选,较好地控制了金属之间的相关性。本研究不足之处在于:1)只采用了尿金属作为金属内暴露的标志物,未检测儿童外暴露水平;2)用BMI定义儿童肥胖,缺少其他反映肥胖的人体测量学指标及生化指标;3)本研究为横断面设计,无法确定金属暴露与肥胖间的因果关系。

综上,湖北省十堰市学龄前儿童部分尿金属水平与儿童的肥胖呈负相关,其中砷和铀可能是肥胖的重要影响因素。

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