

### 【临床研究】

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**Abstract: Objective** To investigate the correlation between 24 h urinary protein quantitation and pregnancy outcome in patients with pre-eclampsia. **Methods** A total of 332 pre-eclampsia patients were selected in Tongji Hospital from January 2014 to December 2016. The patients were divided into microalbuminuria group (24 h urinary protein quantification  $<0.3$  g,  $n=46$ ), mild proteinuria group ( $0.3 \text{ g} \leq 24 \text{ h urinary protein quantification} < 2.0 \text{ g}$ ,  $n=98$ ), moderate proteinuria group ( $2.0 \text{ g} \leq 24 \text{ h urinary protein quantification} < 5.0 \text{ g}$ ,  $n=71$ ) and severe proteinuria group ( $24 \text{ h urinary protein quantification} \geq 5.0 \text{ g}$ ,  $n=117$ ) according to the results of 24 h urinary protein quantification. The pregnancy outcomes were compared between the four groups. **Results** The 24 h urinary protein quantification and the serum creatinine, urea nitrogen, uric acid levels in the mild proteinuria group, moderate proteinuria group and severe proteinuria group were significantly higher than those in the microalbuminuria group ( $P < 0.05$ ); and gestational week was significantly shorter than that in the microalbuminuria group ( $P < 0.05$ ). The 24 h urinary protein quantification and serum urea nitrogen, uric acid levels in the moderate proteinuria group were significantly higher than those in the mild proteinuria group ( $P < 0.05$ ); and gestational week was significantly shorter than that in the mild proteinuria group ( $P < 0.05$ ); but there was no significant difference in serum creatinine level between the two groups ( $P > 0.05$ ). The 24 h urinary protein quantification, serum creatinine, urea nitrogen and uric acid levels in the severe proteinuria group were significantly higher than those in the mild proteinuria group ( $P < 0.05$ ); and the gestational week was significantly lower than that in the mild albuminuria group ( $P < 0.05$ ). The 24 h urinary protein quantification in the severe proteinuria group was significantly higher than that in the moderate proteinuria group ( $P < 0.05$ ), but there was no significant difference in the gestational week and serum creatinine, urea nitrogen, uric acid levels between the two groups ( $P > 0.05$ ). There was no significant difference in the rates of cesarean section and spontaneous labor between the four groups ( $P > 0.05$ ). The rate of induced labor in the moderate proteinuria group and the severe proteinuria group was significantly higher than that in the mild albuminuria group and the microalbuminuria group ( $P < 0.05$ ). There was no significant difference in the rate of induced labor between the mild proteinuria group and the microalbuminuria group ( $P > 0.05$ ). There was no significant difference in the rate of induced labor between the severe proteinuria group and the moderate proteinuria group ( $P > 0.05$ ). The incidence of complications in microalbuminuria group, mild proteinuria group, moderate proteinuria group and severe proteinuria group was 30.43% (14/46), 47.96% (47/98), 74.65% (53/71) and 74.36% (87/117) respectively; the incidence of complications in the moderate proteinuria group and the severe proteinuria group was significantly higher than that in the microalbuminuria group and the mild albuminuria group ( $P < 0.05$ ), but there was no significant difference in the incidence of complications between microalbuminuria group and mild albuminuria group ( $P > 0.05$ ), there was no significant difference in the incidence of complications between the moderate proteinuria group and the severe proteinuria group ( $P > 0.05$ ). The incidences of premature birth and neonatal asphyxia in the mild proteinuria group were significantly higher than that in the microalbuminuria group ( $P < 0.05$ ), and the body mass of the neonates was significantly lower than that in the microalbuminuria group ( $P < 0.05$ ), but there was no significant difference in the perinatal mortality rate and the incidences of fetal growth restriction (FGR) and poor neonatal resuscitation between the two groups ( $P > 0.05$ ). The incidences of FGR, premature birth, neonatal asphyxia, poor neonatal resuscitation and the perinatal mortality in the moderate proteinuria group and severe proteinuria group were significantly higher than those in the microalbuminuria group ( $P < 0.05$ ); and neonatal body mass was significantly lower than that in the microalbuminuria group ( $P < 0.05$ ). The incidences of FGR, premature birth and poor neonatal resuscitation and perinatal mortality in the moderate proteinuria group were significantly higher than those in the mild proteinuria group ( $P < 0.05$ ); and the neonatal body mass was significantly lower than that in the mild proteinuria group ( $P < 0.05$ ); but there was no significant difference in the neonatal asphyxia incidence between the two groups ( $P > 0.05$ ). The incidences of FGR, premature birth, neonatal asphyxia, poor neonatal resuscitation and perinatal mortality in the severe proteinuria group were significantly higher than those in the mild proteinuria group ( $P < 0.05$ ); and the body mass of the newborns was significantly lower than that in the mild albuminuria group ( $P < 0.05$ ). The incidence of neonatal asphyxia in the severe proteinuria group was significantly higher than that in the moderate proteinuria group ( $P < 0.05$ ), but there was no significant difference in the incidences of FGR, premature birth, poor neonatal resuscitation, perinatal mortality and neonatal body mass between the two groups ( $P > 0.05$ ). **Conclusions** The of 24 h urinary protein quantitation is closely related to the pregnancy outcome in patients with pre-eclampsia, the 24 h urinary protein quantification should be regularly detected in the patients with pre-eclampsia. When the urinary protein quantitation is more than 2.0 g, the incidences of maternal complications and poor prognosis of the perinatal infants is significantly higher, but the boundary value of the 24 h urinary protein quantitation for the diagnosis of severe pre-eclampsia still needs further large sample study.

**Key words:** pre-eclampsia; proteinuria; pregnancy outcome

子痫前期是一种妊娠期特发性疾病,发病率 3%~5%<sup>[1-3]</sup>,是导致孕产妇和围生儿死亡的主要原因。子痫前期的主要症状包括高血压、蛋白尿、水肿等。2012 年我国《妊娠期高血压疾病诊治指南》<sup>[4]</sup>将蛋白尿作为诊断子痫前期的必要指标之一,但是 2015 年我国更新了该指南,并下调了蛋白尿在子痫前期诊断中的地位<sup>[5]</sup>,同时世界各国指南中关于尿蛋白对于子痫前期的诊断价值存在争论,亟须进行大规模的研究以指导临床治疗和预测预后。本研究旨在探讨 24 h 尿蛋白定量与子痫前期患者妊娠结局的相关性。

1 资料与方法

1.1 一般资料 选择 2014 年 1 月至 2016 年 12 月华中科技大学同济医学院附属同济医院收治的子痫前期患者,病例纳入标准:(1)符合子痫前期诊断标准<sup>[6]</sup>;(2)单胎妊娠;(3)无妊娠其他并发症。排除标准:既往有高血压、糖尿病及肝肾疾病史患者。共纳入子痫前期患者 332 例,年龄 18~44 岁,平均(30.84±0.28)岁,根据 24 h 尿蛋白定量检测结果分为微量蛋白尿组(24 h 尿蛋白定量<0.3 g)、轻度蛋白尿组(0.3 g≤24 h 尿蛋白定量<2.0 g)、中度蛋白尿组(2.0 g≤24 h 尿蛋白定量<5.0 g)和重度蛋白尿组(24 h 尿蛋白定量≥5.0 g)。微量蛋白尿组 46 例,年龄 22~40 岁,平均(31.78±0.67)岁,平均 24 h 尿蛋白定量(0.18±0.01)g·24 h<sup>-1</sup>。轻度蛋白尿组 98 例,年龄 19~43 岁,平均(32.00±0.52)岁,平均 24 h 尿蛋白定量(0.96±0.05)g·24 h<sup>-1</sup>。中度蛋白尿组 71 例,年龄 21~44 岁,平均(29.99±0.63)岁,平均 24 h 尿蛋白定量(3.17±0.10)g·24 h<sup>-1</sup>。重度蛋白尿组 117 例,年龄 18~44 岁,平均(30.03±0.47)岁,平均 24 h 尿

表 1 4 组患者分娩前肾功能及分娩孕周比较

Tab.1 Comparison of the renal function and gestational week in the four groups before childbirth						( $\bar{x} \pm s$ )
组别	n	尿蛋白定量/(g·24 h <sup>-1</sup> )	肌酐/(μmol·L <sup>-1</sup> )	尿素氮/(mmol·L <sup>-1</sup> )	尿酸/(μmol·L <sup>-1</sup> )	分娩孕周/周
微量蛋白尿组	46	0.18±0.01	54.48±1.53	3.65±0.14	370.50±12.06	37.26±0.24
轻度蛋白尿组	98	0.96±0.05 <sup>a</sup>	67.02±2.89 <sup>a</sup>	4.57±0.24 <sup>a</sup>	402.00±11.90 <sup>a</sup>	35.73±0.30 <sup>a</sup>
中度蛋白尿组	71	3.17±0.10 <sup>ab</sup>	69.03±2.37 <sup>a</sup>	5.33±0.24 <sup>ab</sup>	427.30±12.12 <sup>ab</sup>	33.71±0.42 <sup>ab</sup>
重度蛋白尿组	117	12.30±0.80 <sup>abc</sup>	74.42±2.06 <sup>ab</sup>	5.43±0.22 <sup>ab</sup>	434.60±10.13 <sup>ab</sup>	32.61±0.30 <sup>ab</sup>
F		0.112	8.681	8.201	4.392	4.634
P		<0.05	<0.05	<0.05	<0.05	<0.05

注:与微量蛋白尿组比较<sup>a</sup>P<0.05;与轻度蛋白尿组比较<sup>b</sup>P<0.05;与中度蛋白尿组比较<sup>c</sup>P<0.05。

2.2 4 组患者分娩方式比较 结果见表 2。4 组患者剖宫产率及顺产率比较差异均无统计学意义(P>0.05)。中度蛋白尿组和重度蛋白尿组患者治

蛋白定量(12.30±0.80)g·24 h<sup>-1</sup>。4 组患者的年龄比较差异均无统计学意义(P>0.05)。

1.2 观察指标 查阅患者临床资料,统计记录 4 组患者分娩前血清肌酐、尿素及尿酸水平,分娩方式、分娩周数、早产、胎儿生长受限(fetal growth restriction, FGR)、新生儿体质量、新生儿窒息(出生后 1 min Apgar 评分≤7 分<sup>[7]</sup>)、新生儿复苏不良(出生后 5 min Apgar 评分≤7 分)、围生儿死亡率及母婴并发症(胎盘早剥、眼底病变、胸水、腹水、肝肾功能不全等)。

1.3 统计学处理 应用 SPSS 22.0 软件进行统计分析,计量资料以均数±标准差( $\bar{x} \pm s$ )表示,组间比较采用方差分析和 t 检验,计数资料以百分率表示,采用 $\chi^2$  检验,P<0.05 为差异有统计学意义。

2 结果

2.1 4 组患者分娩前肾功能及分娩孕周比较 结果见表 1。轻度蛋白尿组、中度蛋白尿组和重度蛋白尿组患者 24 h 尿蛋白定量及血清肌酐、尿素氮、尿酸水平显著高于微量蛋白尿组(P<0.05),而分娩孕周显著短于微量蛋白尿组(P<0.05);中度蛋白尿组患者 24 h 尿蛋白定量及血清尿素氮、尿酸水平显著高于轻度蛋白尿组(P<0.05),分娩孕周显著短于轻度蛋白尿组(P<0.05),但 2 组患者血清肌酐水平比较差异无统计学意义(P>0.05);重度蛋白尿组患者 24 h 尿蛋白定量及血清肌酐、尿素氮、尿酸水平显著高于轻度蛋白尿组(P<0.05),而分娩孕周显著短于轻度蛋白尿组(P<0.05);重度蛋白尿组患者 24 h 尿蛋白定量显著高于中度蛋白尿组(P<0.05),但 2 组患者分娩孕周及血清肌酐、尿素氮、尿酸水平比较差异均无统计学意义(P>0.05)。

疗性引产率显著高于轻度蛋白尿组和微量蛋白尿组(P<0.05),但轻度蛋白尿组与微量蛋白尿组患者治疗性引产率比较差异无统计学意义(P>0.05),

重度蛋白尿组与中度蛋白尿组患者治疗性引产率比较差异无统计学意义( $P>0.05$ )。

表 2 4 组患者分娩方式比较

Tab. 2 Comparison of the delivery mode in the four groups				例(%)
组别	<i>n</i>	剖宫产	顺产	治疗性引产
微量蛋白尿组	46	44(95.65)	2(4.35)	0(0.00)
轻度蛋白尿组	98	94(95.92)	2(2.04)	2(2.04)
中度蛋白尿组	71	61(85.92)	0(0.00)	10(14.08) <sup>a</sup>
重度蛋白尿组	117	103(88.03)	0(0.00)	14(11.97) <sup>a</sup>
$\chi^2$		7.581	6.686	14.693
<i>P</i>		>0.05	>0.05	<0.05

注:与轻度蛋白尿组和微量蛋白尿组比较<sup>a</sup> $P<0.05$ 。

表 3 4 组患者并发症发病率比较

Tab. 3 Comparison of the incidence of complications in the four groups								例(%)
组别	<i>n</i>	胎盘早剥	眼底病变	胸水	腹水	肾功能不全	肝功能不全	并发症发生率
微量蛋白尿组	46	0(0.00)	1(2.17)	0(0.00)	8(17.39)	0(0.00)	5(10.87)	14(30.43)
轻度蛋白尿组	98	6(6.12) <sup>a</sup>	2(2.04)	4(4.08)	29(29.59)	13(13.27)	16(16.33)	47(47.96) <sup>a</sup>
中度蛋白尿组	71	5(7.04)	5(7.04)	10(14.08)	26(36.62)	15(21.13)	17(23.94)	53(74.65) <sup>ab</sup>
重度蛋白尿组	117	2(1.71)	15(12.82) <sup>c</sup>	7(5.98)	44(37.61)	30(25.64)	27(23.08)	87(74.36) <sup>ab</sup>

注:与微量蛋白尿组比较<sup>a</sup> $P<0.05$ ;与轻度蛋白尿组比较<sup>b</sup> $P<0.05$ 。

**2.4 4 组围生儿结局比较** 结果见表 4。轻度蛋白尿组早产及新生儿窒息发生率显著高于微量蛋白尿组( $P<0.05$ ),新生儿体质量显著低于微量蛋白尿组( $P<0.05$ ),但 2 组及围生儿死亡率及 FGR、新生儿复苏不良发生率比较差异均无统计学意义( $P>0.05$ )。中度蛋白尿组和重度蛋白尿组 FGR、早产、新生儿窒息和新生儿复苏不良发生率及围生儿死亡率显著高于微量蛋白尿组( $P<0.05$ ),新生儿体质量显著低于微量蛋白尿组( $P<0.05$ )。中度蛋白尿组 FGR、早产和新生儿复苏不良发生率及围生儿死

表 4 4 组围生儿结局比较

Tab. 4 Comparison of the outcomes of perineonates in the four groups

组别	<i>n</i>	FGR/ 例(%)	早产/ 例(%)	新生儿窒息/ 例(%)	新生儿复苏不良/ 例(%)	围生儿死亡/ 例(%)	新生儿 体质量/g
微量蛋白尿组	46	4(8.70)	16(34.78)	8(17.39)	3(6.52)	0(0.00)	2 998.0±157.4
轻度蛋白尿组	98	13(13.27)	61(62.24) <sup>a</sup>	37(37.76) <sup>a</sup>	10(10.20)	5(5.10)	2 642.3±123.8 <sup>a</sup>
中度蛋白尿组	71	19(26.76) <sup>ab</sup>	57(80.28) <sup>ab</sup>	31(43.66) <sup>a</sup>	17(23.94) <sup>ab</sup>	11(15.49) <sup>ab</sup>	1 943.1±192.9 <sup>ab</sup>
重度蛋白尿组	117	26(22.22) <sup>ab</sup>	104(88.89) <sup>ab</sup>	64(54.70) <sup>abc</sup>	31(26.50) <sup>ab</sup>	16(13.68) <sup>ab</sup>	1 933.4±161.3 <sup>ab</sup>

注:与微量蛋白尿组比较<sup>a</sup> $P<0.05$ ;与轻度蛋白尿组比较<sup>b</sup> $P<0.05$ ;与中度蛋白尿组比较<sup>c</sup> $P<0.05$ 。

### 3 讨论

尿蛋白是子痫前期患者肾血管内皮细胞损伤的表现之一,既往各国指南将尿蛋白作为子痫前期的重要诊断指标之一<sup>[4,8-9]</sup>。但是,近年来临床研究表明,一些患者无尿蛋白也会出现子痫前期甚至子痫<sup>[10]</sup>。鉴于此,部分国家包括中国和美国均更新了妊娠期高血压的诊治指南,尿蛋白不再是诊断子痫

**2.3 4 组患者并发症发生率比较** 结果见表 3。微量蛋白尿组、轻度蛋白尿组、中度蛋白尿组和重度蛋白尿组患者并发症发生率分别为 30.43%(14/46)、47.96%(47/98)、74.65%(53/71)、74.36%(87/117),中度蛋白尿组和重度蛋白尿组患者并发症发生率显著高于微量蛋白尿组和轻度蛋白尿组( $P<0.05$ ),微量蛋白尿组与轻度蛋白尿组患者并发症发生率比较差异无统计学意义( $P>0.05$ ),中度蛋白尿组与重度蛋白尿组患者并发症发生率比较差异无统计学意义( $P>0.05$ )。

亡率显著高于轻度蛋白尿组( $P<0.05$ ),新生儿体质量显著低于轻度蛋白尿组( $P<0.05$ ),但 2 组新生儿窒息发生率比较差异无统计学意义( $P>0.05$ )。重度蛋白尿组 FGR、早产、新生儿窒息和新生儿复苏不良发生率及围生儿死亡率显著高于轻度蛋白尿组( $P<0.05$ ),新生儿体质量显著低于轻度蛋白尿组( $P<0.05$ )。重度蛋白尿组新生儿窒息发生率显著高于中度蛋白尿组( $P<0.05$ ),但 2 组 FGR、早产和新生儿复苏不良发生率及围生儿死亡率、新生儿体质量比较差异均无统计学意义( $P>0.05$ )。

前期的必要指标,而加拿大、德国等仍将尿蛋白作为子痫前期诊断的必要条件<sup>[6,11-12]</sup>,而且各国指南对于诊断重度子痫前期的尿蛋白界值并不统一,例如《中国妊娠期高血压诊治指南》中定为 24 h 尿蛋白≥2 g,而德国为≥5 g,即使在中国诊断标准也不尽相同,在《妇产科学》第 8 版中诊断标准为 24 h 尿蛋白≥5 g。由于蛋白尿在子痫前期中的诊断价值及标准存在争议,仍需进一步研究其在预测围生儿

结局及指导终止妊娠时机中的应用价值。

大量蛋白尿可导致低蛋白血症,严重时可促使胸水、腹水的形成,影响孕妇呼吸及循环功能。同时,低蛋白血症还可刺激母体合成脂质及脂蛋白增加,高脂血症可使胎盘动脉粥样硬化,加上胎盘小动脉痉挛,使血流阻力增大,胎盘血流灌注不足,使胎儿长时间处于慢性缺氧状态;还可致使胎儿宫内营养不良,引起 FGR 及胎儿宫内窘迫、新生儿窒息。因此,尿蛋白持续出现会导致子痫前期的进一步加重,可形成恶性循环,故理论上来说,尿蛋白与子痫前期不良围生结局存在相关性。近年来国内外关于尿蛋白与子痫前期不良妊娠结局的相关性研究结果也倾向于二者存在相关性<sup>[13-15]</sup>。

本研究结果显示,随着 24 h 尿蛋白定量的增加,母体并发症和新生儿不良结局的发生率均有升高趋势,分娩孕周呈逐渐减少趋势,新生儿体质量呈逐渐降低趋势。由此可见,24 h 尿蛋白定量与围生结局密切相关,母体并发症和围生儿预后不良发生率随尿蛋白的增加而升高,以 24 h 尿蛋白定量 2 g 为界值时,严重不良妊娠结局发生率大大增加,但与 24 h 尿蛋白定量 5 g 以上患者比较并无显著差异。

综上所述,母体及围生儿不良结局与尿蛋白水平密切相关,应重视子痫前期患者 24 h 尿蛋白定量检测,对病情较重的患者应定期进行 24 h 尿蛋白定量检测,结合其他检查,能更加客观准确地反映子痫前期患者的疾病严重程度并指导合理的治疗,预测围生儿结局,适时终止妊娠,减少严重母体及围生儿并发症的发生。而对于诊断重度子痫前期的 24 h 尿蛋白定量界值,本研究结果显示 2 g 较 5 g 更适合,但是由于本研究样本量较小,尚需大规模、多中心的临床研究进一步证实。

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