

双胎妊娠并发子痫前期的发病趋势、特征及危险因素分析

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摘 要:【目的】探讨双胎妊娠并发子痫前期的发病趋势、特征及危险因素。【方法】回顾性分析2011年1月至2019年12月在中山大学附属第一医院住院分娩的1 542例双胎妊娠孕妇子痫前期的发病趋势。最终1 384例双胎妊娠孕妇纳入后续发病特征及危险因素分析,根据绒毛膜性将其分为单绒毛膜性(monochorionic, MC)组和双绒毛膜性(dichorionic, DC)组,MC共有403例,其中子痫前期(preeclampsia, PE)组55例,非PE组348例;DC共有981例,其中PE组105例,非PE组876例;分别比较不同绒毛膜性孕妇PE组和非PE组的基本资料和分娩结局,采用单因素分析和多因素Logistic回归分析不同绒毛膜性双胎妊娠发生子痫前期的危险因素。【结果】双胎妊娠PE的总发病率为10.4%,2011-2019年各年PE的发病率在7.8%~11.8%之间波动。无论MC与DC双胎妊娠,PE组孕妇贫血(MC为58.2%和39.7%, $P=0.010$;DC为59%和38%, $P=0.000$)、低蛋白血症(MC为7.3%和1.7%, $P=0.035$;DC为10.5%和0.7%, $P=0.000$)、早产(MC为94.5%和70.1%, $P=0.000$;DC为89.5%和54.8%, $P=0.000$)、产后出血(MC为21.8%和10.6%, $P=0.018$;DC为20.9%和13.4%, $P=0.035$)、新生儿转新生儿重症监护室(MC为49.1%和28.6%, $P=0.000$;DC为26.7%和15.6%, $P=0.000$)的发生率均较非PE组高,组间差异有统计学意义;DC双胎妊娠PE组小胎出生体质量和大胎出生体质量均较非PE组轻,组间差异有统计学意义($P=0.000$; $P=0.017$)。孕期增重过多、辅助生殖技术受孕是MC双胎PE的独立危险因素;孕前BMI ≥ 24 kg/m²、孕期增重过多、双胎体质量差过大是DC双胎妊娠PE的独立危险因素。【结论】双胎妊娠PE的发病率波动于7.8%~11.8%;不同绒毛膜性双胎妊娠PE的危险因素和分娩结局略有差异;孕期增重过多、辅助生殖技术受孕、孕前BMI ≥ 24 kg/m²、双胎体质量差过大是双胎妊娠PE的危险因素,提示孕期体质量管理尤为重要。

关键词: 双胎妊娠;子痫前期;危险因素;分娩结局

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Analysis of The Tendency, Characteristic and Risk Factors of Twin Pregnancy Complicated with Preeclampsia

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Abstract:【Objective】To investigate the tendency, characteristic and risk factors of twin pregnancy complicated with preeclampsia.【Methods】A retrospective analysis was performed on the incidence trend of preeclampsia in 1542 twin pregnant women who were hospitalized for delivery in the First Affiliated Hospital of Sun Yat-sen University from January 2011 to December 2019. Finally, 1384 twin pregnant women were included in the analysis of subsequent morbidity characteristics and risk factors, who were divided into Monochorionic (MC) group and Dichorionic (DC) group according to chorionicity. There were 403 MC cases, including 55 cases in Preeclampsia (PE) group and 348 cases in non-PE group and 981 DC

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cases, including 105 cases in PE group and 876 cases in non-PE group. The basic characteristics and delivery outcomes of different chorionic pregnant women in PE group and non-PE group were compared respectively. Univariate analysis and multivariate Logistic regression analysis were used to analyze the risk factors of preeclampsia in different chorionic twin pregnancies.【Results】The total incidence of PE in twin pregnancies was 10.4%, the incidence of PE in twin pregnancies from 2011 to 2019 varied between 7.8% and 11.8%. Regardless of MC and DC twin pregnancies, the incidence of anemia (MC: 58.2% vs 39.7%, $P=0.010$; DC: 59% vs 38%, $P=0.000$), hypoproteinemia (MC: 7.3% vs 1.7%, $P=0.035$; DC: 10.5% vs 0.7%, $P=0.000$), premature delivery (MC: 94.5% vs 70.1%, $P=0.000$; DC: 89.5% vs 54.8%, $P=0.000$), postpartum hemorrhage (MC: 21.8% vs 10.6%, $P=0.018$; DC: 20.9% vs 13.4%, $P=0.035$), neonatal transfer to intensive care unit (MC: 49.1% vs 28.6%, $P=0.000$; DC: 26.7% vs 15.6%, $P=0.000$) in pregnant women in PE group was higher than that in non-PE group, the difference between the two groups were statistically significant. the birth weight of both small fetuses and large fetuses in PE group of DC twins was lower than that in the non-PE group, the difference between these two groups were also statistically significant ($P=0.000$; $P=0.017$). Excessive weight gain during pregnancy and assisted reproductive technology for conception were independent risk factors for MC twin PE. Pre-pregnancy BMI ≥ 24 kg/m², excessive weight gain during pregnancy and excessive weight difference were independent risk factors for PE in DC twins.【Conclusions】The incidence of PE in twin pregnancies fluctuates between 7.8% and 11.8% in each year. The outcomes of PE in different chorionic twin pregnancy are slightly different. Excessive weight gain during pregnancy, assisted reproductive technology for conception, Pre-pregnancy BMI ≥ 24 kg/m² and excessive weight difference of the twins during pregnancy are risk factors for PE in twin pregnancies, suggesting weight management during pregnancy is particularly important.

Key words: twin pregnancy; preeclampsia; risk factors; delivery outcomes

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妊娠期高血压疾病(hypertensive disorder complicating pregnancy, HDCP)是妊娠期特有的并发症,严重威胁母婴健康,在我国的发病率为5%~12%。其中子痫前期-子痫的发病率为2%~8%,是导致孕妇死亡的主要原因之一(占9%~26%)^[1],双胎妊娠属于高危妊娠,较单胎更易引起子痫前期(preeclampsia, PE)、子痫、HELLP综合征等妊娠期合并症及并发症,其PE的发病率是单胎妊娠的3~4倍^[2],且发病迅速,病情较为严重,严重威胁孕妇和围产儿的生命健康,目前终止妊娠是唯一有效的治愈方法。近年来,双胎妊娠的发生率逐年升高,美国的一项全国统计数据显示,2011年双胎妊娠的发生率为3.32%^[3]。国内外关于单胎妊娠PE的危险因素已较为明确,但目前关于双胎妊娠PE危险因素的研究相对较少。本文旨在探讨双胎妊娠并发PE的发病趋势、特征及危险因素,以期将来双胎妊娠并发PE的早期发现与干预提供参考。

1 材料与方 法

1.1 研究对象的纳入、排除标准

纳入标准:收集2011年1月至2019年12月妊

娠 ≥ 20 周并在中山大学附属第一医院住院分娩的所有双胎妊娠孕妇的基本资料、既往史、妊娠合并症与并发症,如:妊娠期糖尿病(gestational diabetes mellitus, GDM)、前置胎盘、妊娠期肝内胆汁淤积症(intrahepatic cholestasis during pregnancy, ICP)、HELLP综合征、贫血、双胎特有的并发症[如双胎输血综合征(twin-twin transfusion syndrome, TTTS)、贫血-多血质序列征(twin anemia-polycythemia sequence, TAPS)、选择性胎儿生长受限(selective fetal growth restriction, sFGR)、双胎生长不一致]及分娩结局的资料。根据绒毛膜性分为MC组与DC组,再按是否发生PE分为PE组与非PE组。PE及重度PE的诊断标准参照妊娠期高血压疾病诊治指南(2020)^[4],胎盘早剥、产后出血、GDM、HELLP综合征、ICP、贫血的诊断参照第9版《妇产科学》^[5];低蛋白血症及弥散性血管内凝血(disseminated intravascular coagulation, DIC)的诊断参照第9版《内科学》^[6];TTTS、TAPS、sFGR、双胎生长不一致的诊断参照双胎妊娠临床处理指南(2020年更新)^[7]。研究已获得本单位伦理委员会批准实施,并取得患者知情同意。

排除标准:妊娠 ≥ 20 周并在中山大学附属第一

医院住院的流产、引产、减胎的双胎妊娠孕妇。

1.2 研究指标

1.2.1 基本资料 孕妇年龄、孕次、产次、孕前体重指数(body mass index, BMI)、分娩前收缩压(systolic pressure, SP)、分娩前舒张压(systolic pressure, DP)、分娩孕周、绒毛膜性、受孕方式、子痫前期的分类、既往史、妊娠合并症与并发症(如GDM、前置胎盘、ICP、HELLP综合征、贫血)、双胎特有的并发症(如TTTS、TAPS、sFGR、双胎生长不一致)。

1.2.2 分娩结局 分娩方式、胎盘早剥、产后出血、DIC、早产、出生体质量、新生儿窒息、新生儿转新生儿重症监护室(neonatal intensive care unit, NICU)、围产儿死亡。

1.3 统计学方法

采用SPSS 20 统计学软件进行分析,两组年龄与孕期增重满足正态性和方差齐性,采用 t 检验,分娩孕周满足正态性不满足方差齐性采用 t' 检验,数据描述以 $(\bar{x} \pm s)$ 表示;两组孕次、产次、孕前BMI、SP、DP、MAP、小胎出生体质量及大胎出生体质量不满足正态性,采用Wilcoxon秩和检验,数据描述以 $M(P_{25} \sim P_{75})$ 表示。妊娠合并症与并发症如GDM、贫血,双胎特有并发症如TTTS、sFGR、双胎生长不一致,分娩结局如产后出血、新生儿窒息、新生儿转新生儿重症监护室发生率的组间比较采用卡方检验;妊娠合并症与并发症如ICP、低蛋白血症,分娩结局如早产、分娩方式、胎盘早剥发生率的组间比较采用Yates卡方检验;妊娠合并症与并发症如前置胎盘、HELLP综合征,双胎特有的并发症TAPS及分娩结局DIC发生率的组间比较采用Fisher确切概率法。单因素分析采用卡方检验或其连续性校正,PE的危险因素分析采用多因素Logistic回归分析,所有统计检验均采用双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 最终纳入研究对象的基本情况

2011–2019年的1 542例双胎妊娠中,发生妊娠期高血压疾病的共209例,占比13.55%,未发生妊娠期高血压疾病的有1 333例,占比86.45%。发生妊娠期高血压疾病的209例中妊娠期高血压34例,占比2.20%,PE 78例,占比56%,重度PE 82例,占比5.30%,妊娠合并慢性高血压8例,占比

0.52%,慢性高血压并发PE 2例,占比0.13%,慢性高血压并发重度PE 5例,占比0.32%。未发生妊娠期高血压的1 333例中109例患妊娠期蛋白尿,占比8.17%。排除妊娠期高血压、妊娠合并慢性高血压、慢性高血压并发PE及重度PE、妊娠期蛋白尿后,最终纳入1 384例双胎孕妇进行分析,包括MC 403例,其中PE组55例(包括PE与重度PE),非PE组348例;DC 981例,其中PE组105例(包括PE与重度PE),非PE组876例;共2 726例活产儿,42例围产儿死亡。双胎妊娠PE的总发病率为10.4%,MC双胎妊娠PE的发病率为12.4%,DC双胎妊娠PE的发病率为9.6%,MC与DC双胎的PE发病率无统计学差异。

2.2 双胎妊娠PE的发病趋势

2011–2019年,双胎妊娠的各年妊娠期高血压疾病发病率依次为12.8%、10%、13%、14.6%、13.8%、12.8%、13.9%、15.2%和16%;PE与重度PE的发病率之和依次为7.8%、9.4%、9.8%、11.8%、10.3%、11.1%、11.3%、10.1%和11.2%,PE的发病率依次为2.8%、5%、6%、6.7%、5.2%、3.8%、4.7%、5.8%和5.3%,重度PE的发病率依次为5%、4.4%、3.8%、5.1%、5.1%、7.5%、6.6%、4.3%和5.9%,各年妊娠期高血压疾病发病率、PE与重度PE的发病率之和、PE与重度PE发病率无统计学差异(表1,图1)。

表1 2011–2019年双胎妊娠期高血压疾病发病率
Table 1 Incidence of hypertensive disorder complicating pregnancy in twin pregnancy from 2011 to

Years	N	2019				[n(%)]
		HDCP	PE	Severe PE	PE and severe PE	
2011	141	18(12.8)	4(2.8)	7(5.0)	11(7.8)	
2012	180	18(10.0)	9(5.0)	8(4.4)	17(9.4)	
2013	184	24(13.0)	11(6.0)	7(3.8)	18(9.8)	
2014	178	26(14.6)	12(6.7)	9(5.1)	21(11.8)	
2015	195	27(13.8)	10(5.2)	10(5.1)	20(10.3)	
2016	187	24(12.8)	7(3.8)	14(7.5)	21(11.1)	
2017	151	21(13.9)	7(4.7)	10(6.6)	17(11.3)	
2018	138	21(15.2)	8(5.8)	6(4.3)	14(10.1)	
2019	188	30(16.0)	10(5.3)	11(5.9)	21(11.2)	

HDCP: hypertensive disorder complicating pregnancy, PE: preeclampsia

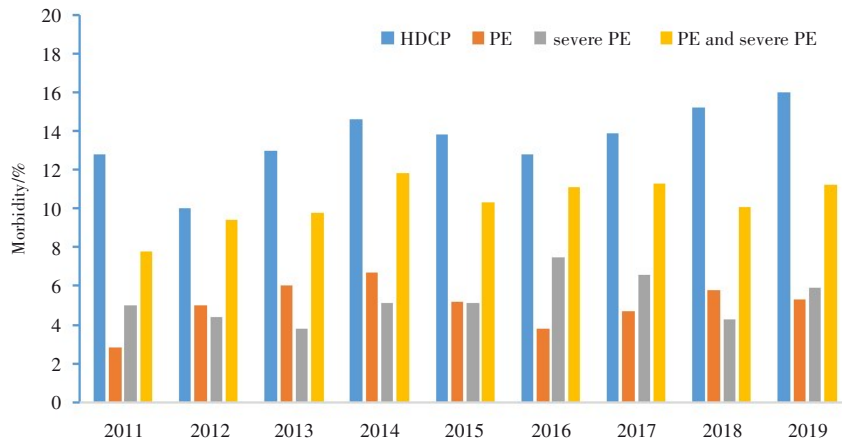


图1 2011~2019年双胎妊娠期高血压疾病发病率

Fig. 1 Morbidity of hypertensive disorder complicating pregnancy in twin pregnancy from 2011 to 2019

2.3 双胎妊娠的基本资料

无论MC还是DC双胎妊娠,与非PE组相比,PE组分娩前SP、DP、MAP均有统计学差异($P=0.000$),MC双胎妊娠中,PE组与非PE组孕次有统计学差异($P=0.035$),DC双胎妊娠中,PE组与非

PE组孕前BMI和分娩孕周(35 ± 2.3 vs 35.9 ± 2)比较,差异有统计学意义($P=0.036, P=0.001$);无论MC还是DC双胎妊娠,PE组与非PE组年龄、产次比较,差异均无统计学意义(表2)。

表2 1384例双胎的基本资料
Table 2 Basic information of 1384 twins $[(\bar{x} \pm s), M(P_{25} \sim P_{75})]$

Basic information	PE group	non-PE group	$t/t'Z$	P
MC ($n=403$)	$n=55$	$n=348$		
Age/years ¹⁾	30.1 ± 5.0	30.8 ± 4.0	1.062	0.289
Gravidity/times ²⁾	1.0 (1.0 ~ 2.0)	2.0 (1.0 ~ 3.0)	-2.105	0.035
Parity/times ²⁾	2.0 (2.0 ~ 3.0)	2.0 (2.0 ~ 3.0)	-1.048	0.295
Pre-pregnancy BMI/(kg/m^2) ²⁾	20.6 (19.2 ~ 22.3)	20.2 (18.6 ~ 22.2)	-1.280	0.201
SP/mmHg ²⁾	138 (127 ~ 146)	118 (110 ~ 126)	-8.925	0.000
DP/mmHg ²⁾	86 (79 ~ 93)	72 (66 ~ 78)	-8.189	0.000
MAP/mmHg ²⁾	102 (96 ~ 109)	87 (81 ~ 93)	-9.093	0.000
Delivery gestations /weeks ³⁾	33.6 ± 2.4	33.8 ± 2.6	0.694	0.490
DC ($n=981$)	$n=105$	$n=876$		
Age/years ¹⁾	31.7 ± 4.4	31.8 ± 3.7	-0.340	0.734
Gravidity/times ²⁾	1.0 (1.0 ~ 2.0)	2.0 (1.0 ~ 2.0)	-1.060	0.289
Parity/times ²⁾	2.0 (2.0 ~ 2.0)	2.0 (2.0 ~ 2.0)	-0.942	0.346
Pre-pregnancy BMI/(kg/m^2) ²⁾	21.2 (19.5 ~ 23.8)	20.1 (19.1 ~ 22.6)	-2.095	0.036
SP/mmHg ²⁾	135 (128 ~ 142)	119 (110 ~ 125)	-12.494	0.000
DP/mmHg ²⁾	85 (77 ~ 91)	73 (68 ~ 78)	-10.732	0.000
MAP/mmHg ²⁾	102 (95 ~ 107)	88 (83 ~ 93)	-12.243	0.000
Delivery gestations /weeks ³⁾	35.0 ± 2.3	35.9 ± 2.0	4.064	0.001

¹⁾ t test, test statistics is t ; ²⁾ Wilcoxon rank sum test, test statistics is Z ; ³⁾ t' test, test statistics is t' ; BMI:body mass index; SP: systolic pressure; DP:diastolic pressure; MAP:mean arterial pressure [$\text{MAP}=(\text{SP}+2\text{DP})/3$].

2.4 双胎妊娠的合并症、并发症与分娩结局

在MC双胎妊娠中,PE组孕妇贫血(58.2% vs 39.7%, $P=0.010$)、低蛋白血症(7.3% vs 1.7%, $P=0.035$)、早产(94.5% vs 70.1%, $P=0.000$)、胎盘早剥(9.1% vs 0.9%, $P=0.000$)、产后出血(21.8% vs 10.6%, $P=0.018$)、新生儿转NICU(49.1% vs 28.6%, $P=0.000$)的发生率均较非PE组高,差异有统计学意义,PE组与非PE组小胎出生体质量比较,差异有统计学意义($P=0.005$);PE组与非PE组GDM、前置胎盘、ICP、HELLP综合征、TTTS、TAPS、sFGR、阴道分娩、剖宫产分娩、DIC、新生儿窒息的发生率和大胎出生体质量无统计学差异。在DC双胎妊娠中,PE组孕妇贫血(59% vs 38%, $P=0.000$)、低蛋白血症(10.5% vs 0.7%, $P=0.000$)、双胎生长不一致(16.2% vs 4.9%, $P=0.000$)、早产(89.5% vs 54.8%, $P=0.000$)、产后出血(20.9% vs 13.4%, $P=0.035$)、新生儿转NICU(26.7% vs 15.6%, $P=0.000$)的发生率均较非PE组高,差异均有统计学意义;PE组与非PE组小胎出生体质量和大胎出生体质量比较,差异有统计学意义($P=0.000$, $P=0.017$);PE组与非PE组GDM、前置胎盘、ICP、HELLP综合征、阴道分娩、剖宫产分娩、胎盘早剥、DIC、新生儿窒息的发生率比较,差异无统计学意义(表3)。

2.5 双胎妊娠PE的单因素分析

在MC双胎妊娠中,PE组辅助生殖技术受孕的发生率较非PE组高(36.4% vs 13.5%, $P=0.000$),孕期增重较非PE组多[(17.8±4.9) kg vs (14.7±4.8) kg, $P=0.000$],差异有统计学意义;而两组年龄≥35岁、初产妇、孕前BMI≥24 kg/m²、孕前BMI≥28 kg/m²、高血压家族史的发生率及双胎体质量差比较,差异无统计学意义;在DC双胎妊娠中,PE组孕前BMI≥24 kg/m²(22.9% vs 13.4%, $P=0.009$)、孕前BMI≥28 kg/m²(4.8% vs 1.5%, $P=0.048$)的发生率较非PE组高,孕期增重较非PE组多[(17.8±6.4) kg vs (14.9±4.9) kg, $P=0.000$]、双胎体质量差较非PE组大($P=0.000$),差异有统计学意义;而两组年龄≥35岁、初产妇、高血压家族史、辅助生殖技术受孕的发生率比较,差异无统计学意义(表4)。

2.6 双胎妊娠PE的多因素分析

MC中有统计学差异的2个因素及DC中有统计学差异的4个因素进行多因素logistic回归分析,结果显示,孕期增重过多、辅助生殖技术受孕是MC双胎PE的独立危险因素;孕前BMI≥24 kg/m²、

孕期增重过多、双胎体质量差过大是DC双胎妊娠PE的独立危险因素(表5、6)。

3 讨 论

3.1 双胎妊娠PE的发病趋势

Rissanen等^[8]的研究表明,2007–2014年间,芬兰双胎妊娠PE与重度PE的发病率之和在13.3%~17.6%之间。Khashan等^[9]提出单胎PE的发病率为2.8%,Sibai等^[10]提出单胎PE与重度PE的发病率之和为4.9%,双胎PE与重度PE的发病率之和较单胎高,为12.7%,双胎重度PE的发病率高达6.4%。本研究结果显示,2011–2019年间,PE与重度PE的发病率之和在7.8%~11.8%之间,较Rissanen等的发病率少,可能是由于近几年医疗条件的改善、医生临床技能的提高有关。本研究的重度PE的发病率在3.8%~7.5%之间,与Sibai等^[10]的研究结果一致。

3.2 不同绒毛膜性双胎合并PE时的妊娠期合并症、并发症与分娩结局

有研究将80例前次妊娠确诊为早发型PE并再次分娩的经产孕妇作为实验组,80例经产孕妇作为对照组,比较两组孕妇孕12周时的外周血血红蛋白量,结果表明实验组外周血血红蛋白低于对照组^[11]。Hou等^[12]选取117例妊娠期高血压单胎孕妇作为病例组,199例健康单胎孕妇作为对照组,发现病例组白蛋白低于对照组。本研究结果显示无论为MC还是DC双胎,PE组双胎孕妇贫血、低蛋白血症的发生率较非PE组高,上述研究为本研究提供了支持证据。早产是双胎妊娠一个较常见的不良妊娠结局,Ananth等^[13]对发达国家的流行病学调查提出双胎妊娠早产的发生率为60%。昆士兰早产临产和分娩指南^[14]提出双胎妊娠早产的发生率为66%。本研究早产的总发病率为62.9%,与多数研究相似。Sibai等^[10]的研究提出双胎PE孕妇早产、胎盘早剥、新生儿转NICU、剖宫产分娩的发生率分别为66.7%、4.7%、42.5%、58.6%;均较单胎PE孕妇高。本研究发现MC双胎PE的早产率高达94.5%,非PE组也达到了70.1%,这可能与MC双胎无论是否发生PE均有较高的双胎特有并发症的发生率有关。本研究双胎PE新生儿转NICU的发生率较Sibai等^[10]略低。总之,无论MC还是DC双胎妊娠,发生PE后,其母儿结

表3 1 384例双胎的并发症及分娩结局

Table 3 Complications and delivery outcomes in 1 384 twins

[n (%), $M(P_{25} \sim P_{75})$]

Complications and delivery outcomes	PE group	non-PE group	χ^2/Z	P
MC ($n=403$)	$n=55$, newborn=110	$n=348$, newborn=696		
GDM ¹⁾	11 (20.0)	72 (20.7)	0.014	0.906
Placenta previa ²⁾	0 (0.0)	2 (0.6)		0.573
ICP ³⁾	1 (1.8)	7 (2.0)	0.009	0.924
HELLP syndrome ²⁾	2 (3.6)	1 (0.3)		0.050
Anemia ¹⁾	32 (58.2)	138 (39.7)	6.684	0.010
Hypoproteinemia ³⁾	4 (7.3)	6 (1.7)	3.967	0.035
TTTS ¹⁾	6 (10.9)	51 (14.7)	0.549	0.459
TAPS ²⁾	2 (3.6)	9 (2.6)		0.657
sFGR ¹⁾	22 (38.6)	102 (29.3)	1.763	0.184
Preterm delivery ³⁾	52 (94.5)	244 (70.1)	14.536	0.000
Vaginal delivery ³⁾	3 (5.5)	22 (6.3)	0.061	0.804
Cesarean delivery ³⁾	52 (94.5)	326 (93.7)	0.061	0.804
Placental abruption ³⁾	5 (9.1)	3 (0.9)	12.570	0.000
Postpartum hemorrhage ¹⁾	12 (21.8)	37 (10.6)	5.564	0.018
DIC ²⁾	1 (1.8)	0 (0.0)		0.136
Neonatal asphyxia ¹⁾	20 (18.2)	101 (14.5)	1.003	0.317
Neonate transfer to NICU ¹⁾	54 (49.1)	199 (28.6)	18.533	0.000
Birth weight of small fetus/kg ⁴⁾	1.6 (1.1 ~ 2.1)	1.9 (1.4 ~ 2.3)	-2.839	0.005
Birth weight of large fetus/kg ⁴⁾	2.1 (1.8 ~ 2.3)	2.2 (1.8 ~ 2.5)	-1.469	0.142
DC ($n=981$)	$n=105$, newborn=210	$n=876$, newborn=1 752		
GDM ¹⁾	22 (21.0)	220 (25.1)	0.874	0.350
Placenta previa ²⁾	1 (1.0)	22 (2.5)		0.500
ICP ³⁾	2 (1.9)	13 (1.5)	0.110	0.670
HELLP syndrome ²⁾	1 (1.0)	0 (0.0)		0.107
Anemia ¹⁾	62 (59.0)	333 (38.0)	17.247	0.000
Hypoproteinemia ³⁾	11 (10.5)	6 (0.7)	47.192	0.000
Discordant fetal growth ¹⁾	17 (16.2)	43 (4.9)	20.783	0.000
Preterm delivery ³⁾	94 (89.5)	480 (54.8)	46.585	0.000
Vaginal delivery	2 (1.9)	20 (2.3)	0.061	0.805
Cesarean delivery ³⁾	103 (98.1)	856 (97.7)	0.061	0.805
Placental abruption ³⁾	4 (3.8)	15 (1.7)	1.207	0.141
Postpartum hemorrhage ¹⁾	22 (20.9)	117 (13.4)	4.449	0.035
DIC ²⁾	1 (1.0)	2 (0.2)		0.288
Neonatal asphyxia ¹⁾	13 (6.2)	66 (3.8)	2.850	0.091
Neonate transfer to NICU ¹⁾	56 (26.7)	273 (15.6)	16.508	0.000
Birth weight of small fetus/kg ⁴⁾	2 (1.6 ~ 2.4)	2.3 (2.1 ~ 2.5)	-4.370	0.000
Birth weight of large fetus/kg ⁴⁾	2.4 (2.1 ~ 2.7)	2.5 (2.3 ~ 2.7)	-2.388	0.017

¹⁾ χ^2 test, test statistics is χ^2 ; ²⁾Fisher's Exact test; ³⁾Yates' adjusted χ^2 test, test statistics is χ^2 ; ⁴⁾Wilcoxon rank sum test, test statistics is Z ; GDM: gestational diabetes mellitus; ICP: intrahepatic cholestasis during pregnancy; TTTS: twin-twin transfusion syndrome; TAPS: twin anemia-polycythemia sequence; sFGR: selective fetal growth restriction; NICU: neonatal intensive care unit.

表4 双胎PE的单因素分析结果

Table 4 Single factor analysis results of twin PE $[(\bar{x} \pm s), n(\%), M(P_{25} \sim P_{75})]$

Items	PE group	non-PE group	$\chi^2/t/Z$	P
MC(n=403)	n=55	n=348		
Age \geq 35year old ¹⁾	11 (20.0)	59 (17.0)	0.307	0.580
Primipara ¹⁾	41 (74.5)	233 (67.0)	1.258	0.262
Pre-pregnancy BMI \geq 24 kg/m ² ¹⁾	8 (14.5)	39 (11.2)	0.514	0.473
Pre-pregnancy BMI \geq 28 kg/m ² ²⁾	2 (3.6)	6 (1.7)	0.180	0.671
Family history of hypertension ¹⁾	7 (12.7)	39 (11.2)	0.109	0.742
Assisted reproductive technology ¹⁾	20 (36.4)	47 (13.5)	17.902	0.000
Gestational weight gain/kg ³⁾	17.8 \pm 4.9	14.7 \pm 4.8	-4.477	0.000
Weight difference of the twins /kg ⁴⁾	0.20 (0.09 ~ 0.51)	0.38 (0.21 ~ 0.63)	-1.827	0.068
DC (n=981)	n=105	n=876		
Age \geq 35year old ¹⁾	30 (28.6)	205 (23.4)	1.376	0.241
Primipara ¹⁾	89 (84.8)	708 (80.8)	0.966	0.328
Pre-pregnancy BMI \geq 24 kg/m ² ¹⁾	24 (22.9)	117 (13.4)	6.877	0.009
Pre-pregnancy BMI \geq 28 kg/m ² ²⁾	5 (4.8)	13 (1.5)	3.921	0.048
Family history of hypertension ¹⁾	16 (15.2)	100 (11.4)	1.314	0.252
Assisted reproductive technology ¹⁾	75 (71.4)	591 (67.5)	0.675	0.411
Gestational weight gain/kg ³⁾	17.8 \pm 6.4	14.9 \pm 4.9	-5.479	0.000
Weight difference of the twins/kg ⁴⁾	0.16 (0.08 ~ 0.30)	0.29 (0.17 ~ 0.59)	-5.298	0.000

¹⁾ χ^2 test, test statistics is χ^2 ; ²⁾Yates' adjusted χ^2 test, test statistics is χ^2 ; ³⁾t test, test statistics is t; ⁴⁾Wilcoxon rank sum test, test statistics is Z.

表5 MC并发PE危险因素的logistic回归分析

Table 5 Logistic regression analysis of risk factors for MC concurrent PE

Variables	β	Wald χ^2	P	OR	OR 95%CI	
					lower	upper
Gestational weight gain/kg	0.137	17.709	0.000	1.147	1.076	1.223
Assisted reproductive technology	0.145	11.720	0.001	1.157	1.064	1.257

表6 DC并发PE危险因素的logistic回归分析

Table 6 Logistic regression analysis of risk factors for DC concurrent PE

Variables	β	Wald χ^2	P	OR	OR 95%CI	
					lower	upper
Pre-pregnancy BMI \geq 24 kg/m ²	0.835	7.557	0.006	2.305	1.271	4.180
Gestational weight gain/kg	0.096	18.772	0.000	1.101	1.054	1.150
Weight difference of the twins /kg	0.854	11.108	0.000	2.348	1.421	3.879

局均较差,因此探讨双胎妊娠发生PE的危险因素并及早识别和采取相应的预防措施尤为重要。

3.3 孕前体质量、孕期增重对双胎妊娠PE发病的影响

根据中国人口的标准, BMI \geq 24 kg/m²或 BMI \geq

28 kg/m²分别被定义为超重或肥胖。Lucovnik等^[15]纳入3 885例双胎妊娠孕妇进行病例对照研究,结果显示孕前超重(BMI为25~29.9 kg/m²)和肥胖(BMI \geq 30 kg/m²)与PE的发生有关;2014年,其又提出双胎妊娠PE与孕期BMI变化无关。而Gavard

等^[16]的研究表明孕期增重过多的孕妇PE的发病风险增加。Fox等^[17]的研究表明孕前肥胖可增加双胎孕妇产前1.367倍的发生风险。耿小妍等^[18]回顾性分析了1 297例双胎妊娠孕妇,提出孕期增重过多会增加PE的风险。本研究发现孕期增重过多是PE的危险因素,与大多数研究一致。这提示孕期体质量的管理尤为重要,因此应做好孕期体质量的评估,制定孕期个体化的体质量管理方案,做好孕期体质量管理的健康宣教,力求达到孕期体质量的合理增长^[19]。

3.4 辅助生殖技术对双胎妊娠PE发病的影响

Lynch等^[20]纳入528例多胎妊娠孕妇,评估辅助生殖技术与多胎妊娠PE的关系,结果显示辅助生殖技术的多胎孕妇PE的发生风险是自然受孕的2.1倍。Fox等^[17]的研究表明辅助生殖技术是非高龄初产妇双胎妊娠PE发生的独立危险因素,其中卵子捐赠是双胎妊娠PE发生的危险因素。这可能与辅助生殖技术术前应用各种卵泡刺激药物及术后应用黄体支持药物而造成的体内环境变化有关^[21]。但也有研究提示,除剖宫产率及早产率增加以外,辅助生殖技术并不增加妊娠期高血压疾病等母体疾病^[22]。本研究发现辅助生殖技术受孕

与MC双胎孕妇PE的发生有关而与DC双胎的发生无关,这可能与本研究纳入的PE孕妇样本量较少有关。因此应进行更多的大样本研究来明确辅助生殖技术受孕对不同绒毛膜性双胎PE的影响是否有差异。

3.5 双胎体质量差对双胎妊娠PE的影响

有研究表明在sFGR中,PE的发生率明显高于正常生长的双胎妊娠(OR值为3.29)^[23]。两个胎儿估测体质量差异 $\geq 25\%$ 是sFGR或双胎生长不一致的诊断标准之一^[7],双胎体质量差大的双胎妊娠孕妇更容易并发PE。本研究发现双胎体质量差较大为DC双胎PE的一个危险因素,与MC双胎妊娠略有差异。但由于PE组的样本量相对较少,应进行进一步研究明确这种差异的可靠性。因此,产科医生在孕期应定期进行超声检查评估双胎体质量,早期发现双胎的体质量异常并采取相应的干预手段,尽最大可能减少母儿不良结局。

总之,对于有发生PE危险因素的双胎孕妇,产科医生应对孕期增重、孕前体质量等可控因素给予指导、干预,对双胎体质量等相关指标进行监测,以期降低双胎孕妇PE的发生率及减少其母儿不良妊娠结局,最大程度地保证母儿安全。

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