Effect of epidural labor analgesia on postpartum depression and maternal and infant outcomes in parturients with gestational diabetes mellitus—A prospective cohort study

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Abstract

Background

Postpartum depression (PPD) negatively affects the health of new mothers and can impair infant development. Both labor pain and gestational diabetes mellitus (GDM) are potential risk factors for PPD. However, the effects of epidural labor analgesia in parturients with GDM on PPD and maternal and infant outcomes have not been characterized.

Methods

Parturients with GDM in our hospital were assigned to the epidural group (n = 133) and no epidural (control) group (n = 130) according to their choice to receive epidural labor analgesia. The Edinburgh Postnatal Depression Scale (EPDS) was used to evaluate maternal mental status at 24 h and 42 days postpartum. Data for relative variables in the perinatal period were collected, and the potential associations of epidural analgesia with PPD and maternal and infant outcomes were analyzed by univariate analysis and multivariate logistic regression analyses.

Results

Epidural analgesia was a protective factor for PPD at 24 h postpartum (odds ratio [OR], 0.301, 95% confidence interval [CI]: 0.104–0.867, $p < 0.05$), and the EPDS score at 24 h post-delivery showed significant correlation with that at 42 days post-delivery (Pearson correlation coefficient = 0.527, $p < 0.001$). The rate of neonatal admission to the neonatal intensive care unit (NICU) for hypoglycemia was higher in the epidural group (6.92%) than in the control group (1.50%; $p < 0.05$). Epidural analgesia and drug-based diabetes control were independent predictors of the rate of neonate transfer to the NICU for hypoglycemia.

Conclusion

Epidural analgesia was a protective factor for PPD at 24 h postpartum, but associated with an increased risk of neonatal transfer to the NICU for hypoglycemia. Thus, monitoring of neonatal blood glucose levels after administration of epidural analgesia in parturients with GDM may be beneficial.

Clinical Trial Registration

the study was registered in the China Clinical Registration Center (URL: http://www.chictr.org.cn/listbycreater.aspx, Registration No. ChiCTR-OOC-17013164)

Background

Gestational diabetes mellitus (GDM) refers to impaired glucose metabolism appearing during pregnancy [1] and is now one of the most common complications of pregnancy. In many countries, including

developing countries, the morbidity of GDM has increased over 30% in the last two decades [2]. The occurrence of GDM is caused by a variety of factors and associated with increased risks of several adverse outcomes for both mothers and infants, including gestational hypertension, intrauterine death and perinatal asphyxia [3], macrosomia [4], premature delivery [5], and neonatal hypoglycemia [6]. Long-term adverse effects on mothers and infants are also possible, with research showing that parturients with GDM have an increased risk of type 2 diabetes and their offspring have an increased risk of obesity [7].

Labor pain induces a neuroendocrine response to stress that can cause a series of physiological changes, including increases in cortisol and blood glucose levels. In parturients with GDM, this can aggravate blood glucose fluctuation, causing further metabolic disorder that can have adverse effects on the fetus. Accordingly, researchers have investigated the benefits of labor analgesia in these patients and reported that it can relieve this stress response in parturients [8] and benefit the control of blood glucose and cortisol levels [9].

Postpartum depression (PPD) is a common mental disorder. Estimates of its incidence worldwide have ranged from 11–19.2% [10–15], while estimates of its incidence in China have ranged from 6.7–34.6% [16–19]. Studies have shown that PPD can negatively affect early breastfeeding and lead to a strained mother–infant relationship [20, 21] and can also have detrimental effects on the long-term cognitive, social interaction, emotional, and physical development of infants [22–25]. The causes of PPD remain incompletely understood, although correlations between several factors and the occurrence of PPD have been identified. For example, the severity of pain during childbirth was shown to correlate with the occurrence of early PPD [26]. Indeed, pain often co-occurs with depression, and emerging evidence suggests an association between pain and PPD [27]. While labor pain is the main cause of adverse emotions during delivery, it remains controversial whether labor analgesia can reduce the incidence of PPD. Some studies have reported a lower incidence of PPD in patients who received epidural analgesia during delivery [16, 28, 29], while other studies did not find that labor analgesia reduced the incidence of PPD [9, 12, 30]. O'Hara and Swain found that marital difficulties, life stress, prenatal depression, lower socioeconomic status, increased body mass index (BMI), and a history of abuse were all associated with an increased risk of PPD [11]. Multiple studies have also demonstrated that GDM is an independent risk factor for PPD [31–33]. Alterations in metabolic status, inflammation, and hypothalamus-pituitary-adrenal function may explain the potential relationship between GDM and PPD [34–36].

Although these various correlations have been reported, the effects of epidural labor analgesia on the occurrence of PPD among pregnant women with GDM as well as on maternal and infant outcomes have not been determined. Therefore, the present prospective observational cohort study was designed to investigate whether epidural labor analgesia is associated with the risk of PPD in women with GDM and to examine its impact on maternal and infant outcomes, including those related to the labor process, side effects, mode of delivery, birth details, and infant health.

Methods

Study participants

Patients were recruited in Shenzhen Maternity and Child Healthcare Hospital from January 2018 to October 2019. The inclusion criteria were: a diagnosis of GDM according to the diagnostic standard of IADPSG 2010 [37] (fasting blood glucose of 5.1–7.1 mmol/L or any blood glucose level reaching or exceeding the following criteria on a 75-g oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation: fasting blood glucose < 5.1 mmol/L, 1-h blood glucose < 10.0 mmol/L, and 2-h blood glucose < 8.5 mmol/L); gestational age at delivery ≥ 35 weeks; and single fetal head position consistent with vaginal delivery. Patients were excluded if they refused participation or had: a neurological or mental disease; contraindications for intraspinal anesthesia (e.g., nerve injury symptoms during pregnancy, history of lumbar spine disease, systemic infection, and blood disease); a serious cardiovascular disease; a liver or kidney disease; or an endocrine disease other than GDM. Parturients were admitted into a delivery room when cervical dilation reached 3 cm for first-time mothers or 2 cm for mothers who had previously delivered a child. All eligible parturients were informed of the study and were included only after they provided written informed consent. Epidural labor analgesia was administered solely based upon the wishes of the parturient.

The study was conducted in accordance with the Declaration of Helsinki and Chinese clinical trial research regulations. The study protocol was approved by the Shenzhen Maternity and Child Healthcare Hospital Ethics Committee (Approval No. SZFY2017102095). Written informed consent was obtained from all enrolled parturients, and the study was registered in the China Clinical Registration Center (Registration No. ChiCTR-OOC-17013164).

Data collection

The following basic demographic and clinical data were obtained for parturients by questionnaire, medical records review, and oral interview: age, height, weight, gestational week, parity, medical history (adverse pregnancy history, obstetric complications), smoking and alcohol consumption habits, long-term medication use during pregnancy, pregnancy-related information (planned or unplanned pregnancy, source of health information during pregnancy), family environment and marital status (education level of mother and father, family income, number of siblings of parturient, marital history, marital relationship during pregnancy, father's satisfaction with the infant's sex, members of the parturient's household), mental state during pregnancy, work-related information (occupation, maternity leave time, effects of childbirth on work or re-employment), and clinical details of GDM including the method of blood glucose control diabetes (diet or medication).

The following delivery-related data were recorded: administration of epidural labor analgesia, stage duration, mode of delivery, and adverse events during delivery (pruritus, dizziness, chills, nausea, vomiting, urine retention). The Numerical Rating Scale (NRS) was used to characterize pain during delivery. With this scale, the patient rates their degree of pain by reported a number from 0 to 10, where 0 represents no pain and 10 represents the most serious pain [38].

The following neonatal clinical data were recorded: sex, body weight, 1- and 5-min Apgar scores, and heel blood glucose levels at 1, 2 and 3 h after birth. A blood glucose level less than 2.6 mmol/l is considered the limit value for clinical treatment of hypoglycemia [39]. Therefore, the blood glucose level was rechecked if < 2.6 mmol/L, and a repeated abnormal level prompted transfer to the neonatal intensive care unit (NICU) for treatment of hypoglycemia. The husband's preference for the infant's sex was investigated on the second day after delivery [19].

Epidural labor analgesia

Epidural analgesia was performed at the L2-3 epidural space. After the administration of lidocaine at a test dose to exclude intravascular and subarachnoid injection, local anesthetics (0.125% ropivacaine and 0.4 μg/ml sufentanil) in a 10-ml loading dose were administered. After the effect of analgesia was confirmed, a patient-controlled epidural analgesia (PCEA) pump was connected (0.1% ropivacaine + sufentanil 0.4 μg/ml, background dose of 5 ml/h, PCEA dose of 5 ml/bolus, locking time of 15 min, and maximum dose of 23 ml/h). The PCEA pump was used until delivery. If the patient reported a NRS score > 4, an additional 5-ml bolus was administered by the anesthetic nurse. NRS scores were recorded pre-epidural analgesia and at cervical dilation of 5cm and 10 cm. Parturients' blood pressure was monitored, and if hypotension (decrease by > 30% baseline) appeared, norepinephrine was administered, and if bradycardia (heart rate < 60 bpm) occurred, atropine was administered.

Postpartum assessment

Maternal depression was assessed using the Edinburgh Postpartum Depression Scale (EDPS) at 24 h and 42 days after delivery [40, 41]. In the present study, PPD was defined as a EPDS score ≥ 10 at 42 days after delivery. The EPDS questionnaire contains 10 items, which are scored from 0 to 3 according to the severity of symptoms. The maximum total score is 30 points, and 10 points is the scoring standard for identifying PPD with great clinical significance [41]. At 24 h after delivery, the mental status of parturients was evaluated using the Zung Self-Rating Anxiety Scale (SAS) [42] to assess the patient's anxiety level and the Social Support Rating Scale (SSRS [43] to assess the patient's social support level. Additional information gathered during the telephone follow-up at 42 days after delivery included: the recovery of blood glucose control, the presence of chronic pain or other special conditions, the health status of the newborn, the feeding patterns of the newborn, and details of the mother's living arrangement (whether living with parent-in-law).

Sample size calculation and data analysis

The main index for the present study was the incidence of PPD at 42 days after delivery. For the sample size calculation for two independent groups, we presumed that equal numbers of patients would be assigned to the two groups, as the rate of labor analgesia use in our hospital in 2017 was 48.5%. PPD was assumed as a binary result, and we assumed PPD incidence rates of 10% in the epidural labor analgesia group and of 25% in the non-epidural labor analgesia group according to the literature.[16, 28, 30] For 80% power and 0.05 two-tailed significance, the sample size needed for each group was

calculated to be 100 by the Power Analysis and Sample Size (PASS) 2011 software (NCSS, LLC). To compensate for 20% loss to follow-up, 120 patients were needed in each group.

All statistical analyses were performed using SPSS version 25.0 software. The quantitative data were described as mean ± standard deviation or median (quartile) according to whether the data obeyed a normal distribution, and the significance of differences between groups was determined by t test or rank sum test. Counting data were described as frequency (constituent ratio), and the significance of differences between groups was determined by chi square test or Fisher exact probability test. Univariate analysis was conducted, and all factors identified as significant were included in a multivariate logistic regression analysis to analyze the relationships of 24-h and 42-day EDPS scores with epidural labor analgesia, age, BMI, SAS score, and SSRS score as well as the relationships of NICU transfer for hypoglycemia with epidural labor analgesia, age, and BMI. Epidural analgesia was set as the dependent variable, and the variables that showed a statistically significant difference between the two groups were set as independent variables. The 1:1 nearest neighbor matching method was used, and the caliper value was set to 0.02. Propensity score matching was performed, and the matched data were analyzed by the same analysis strategy to identify significant relationships of 24-h and 42d EDPS scores and NICU transfer for hypoglycemia with other variables. For all statistical tests, significance was defined as a two-tailed p value < 0.05.

Results

Demographic and clinical characteristics of enrolled parturients

A flow chart outlining the study enrollment process is presented in Fig. 1. Of a total of 372 eligible parturients, 68 were excluded according to the exclusion criteria. Of the 304 patients enrolled in the study, 3 patients refused participation in the 24-h follow-up, and 38 patients were lost to the 42-day follow-up. Thus, the final analysis included 263 parturients. With 130 patients in the epidural labor analgesia group (hereafter, epidural group) and 133 in the no epidural labor analgesia group (hereafter, control group), the rate of epidural labor analgesia use was 49.43%.

The demographic data of the patients in each group are presented in Table 1. Patient age, history of abnormal pregnancy, and SSRS score were lower in the epidural group than in the control group (all $p < 0.05$). Additionally, the epidural group included more primiparae and fewer multiparae compared with the control group ($p = 0.000$). More women in the epidural group reported occupations of business\service and housewife than in the control group (both $p < 0.05$). No significant differences in height, weight, BMI, gestational age at delivery, and SAS score were observed between the groups.

Table 1
Baseline demographic and obstetric characteristics of parturients who completed the study

Characteristic	Epidural group (n = 130)	No epidural (control) group (n = 133)	p
Ages (years)	30.35 ± 3.81	32.74 ± 4.12	0.000
Height (cm)	159.08 ± 5.02	159.34 ± 5.08	0.675
Weight (kg)	62.05 ± 8.14	61.59 ± 10.78	0.698
Body mass index (kg/m^2)	24.50 ± 2.89	24.24 ± 3.97	0.546
Gestational age at delivery (weeks)	39.12 ± 0.86	38.94 ± 0.96	0.110
Gravidity			
Primipara	87 (66.92%)	31(23.31%)	0.000
Multipara	43(33.08%)	102(76.69%)	0.000
Parental education			
Maternal education > 12 y	105(80.77%)	96(72.18%)	0.111
Husband education > 12 y	110(84.62%)	100(75.19%)	0.666
Family income (¥/mo)a			
< 3000	0 (0%)	2(1.50%)	0.498
3000–6000	16(12.31%)	21(15.79%)	0.48
6000–10000	47(36.15%)	51(38.35%)	0.799
10000–20000	44(33.85%)	36(27.07%)	0.248
> 20000	23(17.69%)	23(17.29%)	0.511

Data are presented as mean ± SD, number of patients (percentage), or median (range).BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; SD: standard deviation; ¥ = Chinese Yuan.

[a]Total income of husband and wife.

[b]Abnormal pregnancy included embryo termination, fetal malformation, stillbirth, stillbirth history, postpartum hemorrhage, ectopic pregnancy, etc.

[c]Obstetric diseases included pregnancy-induced hypertension syndrome, low free triiodothyronine and free thyroxine during pregnancy.

Comparisons were made using Student's t-test or Wilcoxon rank sum test for non-normally distributed variables or using Pearson's chi-squared test and Fisher's exact test for proportions.

Characteristic	Epidural group (n = 130)	No epidural (control) group (n = 133)	p
Occupation			
Office worker	50(38.46%)	51(38.35%)	1.000
Professional	14(10.77%)	13(9.77%)	0.841
Business\service	10(7.69%)	0(0%)	0.001
Self-employed	8(6.15%)	18(13.53%)	0.062
Migrant worker	8(6.15%)	10(7.52%)	0.808
Housewife	15(11.54%)	4(3.01%)	0.008
Others	25(19.23%)	37(27.82%)	0.111
Source of health knowledge during pregnancy			
Routine obstetric examination	127(97.69%)	132(99.25%)	0.366
Maternity classes	99(76.15%)	100(75.19%)	0.886
Internet resources or books	124(95.38%)	128(96.24%)	0.767
Maternity leave time			
None	11(8.46%)	9(6.77%)	0.648
Legal time	101(77.69%)	114(85.71%)	0.111
Full-time	18(13.85%)	10(7.52%)	0.112
Maternal situational factors			
Childbirth affects work or re-employment	19(14.62%)	14(10.53%)	0.355

Data are presented as mean ± SD, number of patients (percentage), or median (range).BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; SD: standard deviation; ¥ = Chinese Yuan.

[a]Total income of husband and wife.

[b]Abnormal pregnancy included embryo termination, fetal malformation, stillbirth, stillbirth history, postpartum hemorrhage, ectopic pregnancy, etc.

[c]Obstetric diseases included pregnancy-induced hypertension syndrome, low free triiodothyronine and free thyroxine during pregnancy.

Comparisons were made using Student's t-test or Wilcoxon rank sum test for non-normally distributed variables or using Pearson's chi-squared test and Fisher's exact test for proportions.

Characteristic	Epidural group (n = 130)	No epidural (control) group (n = 133)	p
Unplanned pregnancy	26(20.00%)	31(23.31%)	0.552
History of abnormal pregnancy[b]	28(21.54%)	49(36.84%)	0.007
Pregnancy with obstetric disease[c]	11(8.46%)	13(9.77%)	0.831
Anxiety and depression during pregnancy	7(5.38%)	9(6.77%)	0.798
History of depression and trauma	2(1.54%)	1(0.75%)	0.619
Cigarette, alcohol, long-term medication use during pregnancy	0(0%)	1(0.75%)	1.000
Parturient is only child	21(16.15%)	18(13.53%)	0.605
Remarried	3(2.31%)	4(3.01%)	1.000
Husband satisfied with infant's sex	0(0%)	2(1.5%)	0.498
Changes in marital relationship during pregnancy	4(3.08%)	1(0.75%)	0.210
Method for diabetes control			
Diet	121(93.08%)	119(89.47%)	0.384
Medication	9(6.92%)	14(10.53%)	0.384
Maternal blood glucose control during pregnancy (Normal)	109(83.85%)	112(84.21%)	1.000
SAS score	37.32 ± 8.38	36.52 ± 7.36	0.407
SSRS score	41.72 ± 8.67	45.35 ± 7.60	0.000

Data are presented as mean ± SD, number of patients (percentage), or median (range).BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; SD: standard deviation; ¥ = Chinese Yuan.

[a]Total income of husband and wife.

[b]Abnormal pregnancy included embryo termination, fetal malformation, stillbirth, stillbirth history, postpartum hemorrhage, ectopic pregnancy, etc.

[c]Obstetric diseases included pregnancy-induced hypertension syndrome, low free triiodothyronine and free thyroxine during pregnancy.

Comparisons were made using Student's t-test or Wilcoxon rank sum test for non-normally distributed variables or using Pearson's chi-squared test and Fisher's exact test for proportions.

Effect of epidural labor analgesia on the occurrence of PPD, labor pain, adverse effects during delivery, and the rate of vaginal delivery

The incidence of an EDPS score at 24 h after delivery of ≥ 10 was 15.38% (20/130) in the epidural group and 18.80% (25/133) the in the control group, and no significance difference was detected between the groups ($p = 0.463$). An EDPS score ≥ 10 was detected in two more patients in the epidural group at 42 days after delivery than at 24 h post-delivery (22/130, 16.92%), whereas an EDPS score ≥ 10 was detected in 10 fewer patients in the control group at 42 days compared with 24 h post-delivery (15/133, 11.28%). Still at 42 days after delivery, the incidence of an EDPS score ≥ 10 did not differ significantly between the two groups ($p = 0.284$). A significant correlation was found between the EPDS score at 24 h postpartum and that at 42 days after delivery (Pearson correlation coefficient = 0.527, $p < 0.001$).

As expected, the NRS scores for pain when cervical dilation reached 5 cm and 10 cm were significantly lower in the epidural group than in the no epidural control analgesia group ($p = 0.000$). We also observed that the durations of the first and second stages of labor were longer in the epidural group than in the control group ($p = 0.000$). Regarding adverse effects, the percentages of patients who experienced itching, dizziness, and urinary retention were significantly higher in the epidural group than in the control group (Table 2).

Table 2
Perinatal variables of parturients who completed the study

Variable	Epidural group (n = 130)	No epidural (control) group (n = 133)	p
NRS score	8.98 ± 1.77	8.86 ± 1.64	0.789
Baseline			
At cervical dilation 5 cm	3.21 ± 1.91	9.01 ± 1.79	0.000
At cervical dilation 10 cm	3.69 ± 1.87	9.23 ± 1.24	0.000
Duration of labor (min)	594.52 ± 32.01	202.46 ± 13.99	0.000
Stage 1			
Stage 2	52.68 ± 46.27	18.98 ± 20.13	0.000
Stage 3	9.63 ± 6.45	9.46 ± 5.80	0.820
Adverse effects during delivery			
Itch	8(6.02%)	1(0.75%)	0.018
Dizzy	24(18.46%)	13(9.77%)	0.043
Nausea	7(5.38%)	7(5.26%)	0.965
Vomiting	9(6.92%)	3(2.26%)	0.070
Chills	26(20.0%)	17(12.78%)	0.114
Urinary retention	11(8.46%)	1(0.75 %)	0.030
Mode of delivery			
Vaginal birth	130(100%)	131(98.5%)	0.498
Cesarean	0(0%)	2(1.5%)	0.498
EPDS score at 24 h after delivery	6.24 ± 3.38	6.33 ± 3.87	0.837
EPDS score at 24 h ≥ 10	20(15.38%)	25(18.80%)	0.463
EPDS score at 42 days after delivery	5.91 ± 3.18	5.38 ± 3.53	0.207
EPDS score at 42 days ≥ 10	22(16.92%)	15(11.28%)	0.284
Data are presented as mean ± SD, number of patients (percentage), or median (range).			
NRS = Numeric Rating Scale; EPDS = Edinburgh Postnatal Depression Scale. Comparisons were made using Student's t-test or Wilcoxon rank sum test for non-normally distributed variables and using Pearson's chi-squared test and Fisher's exact test for proportions.			

Vaginal delivery was achieved by all parturients in the epidural group (100%) and by 98.5% of parturients in the control group (131/133). No significant difference in the rate of vaginal delivery was observed between the two groups (p = 0.199; Table 2).

Effect of epidural labor analgesia on neonatal variables

When neonatal health outcomes were compared between the epidural group and no epidural control group, no significant differences in the infants' weight, sex, and 1-min and 5-min Apgar scores were observed between the groups (Table 3). However, the incidence of newborn hypoglycemia (< 2.6 mmol/L) was higher in the epidural group than in the control group at both 2 h (5.38% [7/130] vs. 0.75% [1/133], p = 0.035) and 3 h (6.92% [9/130] vs. 1.50% [2/133], p = 0.028) after delivery. Twenty-six newborns were transferred to the NICU (1 for congenital malformation, 1 for congenital pericardial effusion, 9 for mild asphyxia, 1 for jaundice, 2 for low birth weight, 2 for maternal fever, 1 for macrosomia, and 9 for hypoglycemia) in the epidural group, and 14 newborns were transferred to the NICU (7 for mild asphyxia, 4 for low birth weight, 1 for anemia, and 2 for hypoglycemia) in no epidural control group. The percentage of newborns who required NICU care for hypoglycemia was 6.92% (9/130) in the epidural group compared with only 1.50% (2/133) in the control group (p = 0.028).

Table 3
Health outcomes for newborns of parturients enrolled in this study

Neonatal outcomes	Epidural group (n = 130)	No epidural (control) group, (n = 133)	p
Neonatal weight (g)	3279 ± 405	3189 ± 469	0.099
Neonatal weight ≧ 3500 g	35(26.92%)	30(22.55%)	0.475
Neonatal gender	78(60.0%)	72(54.14%)	0.337
Male			
Female	52(40.0%)	61(45.86%)	0.337
Apgar score	10(7–10)	10(9–10)	0.983
1 min			
5 min	10(10–10)	10(10–10)	0.324
Heel blood glucose after birth			
< 2.6 mmol/L at 1 h	15(11.54%)	8(6.02%)	0.115
< 2.6 mmol/L at 2 h	8(6.15%)	1(0.75%)	0.035
< 2.6 mmol/L at 3 h	7(5.38%)	2(1.50%)	0.028
NICU admission after birth	26(20.0%)	14(10.53%)	0.030
NICU admission after birth for hypoglycemia treatment	9(6.92%)	2(1.50%)	0.028

Data are presented as number of patients (percentage), mean ± SD, or median (range). Comparisons were made using Student's t-test or Wilcoxon rank sum test for non-normally distributed variables or using Pearson's chi-squared test and Fisher's exact test for proportions.

Factors associated with the occurrence of PPD

When PPD at 24 h after delivery was used as a dependent variable, univariate logistic regression analysis identified a total of five significant maternal and neonatal variables: anxiety and depression during pregnancy, unplanned pregnancy, maternal blood glucose control during pregnancy, SAS score, and SSRS score ($p < 0.05$). Of these factors, two were identified as significantly associated with PPD at 24 h after delivery on multivariate logistic regression analysis, the SAS and SSRS scores at 24 h after delivery (Table 4).

Table 4
Results of univariate and multivariate analyses of factors associated with PPD at 24 h after delivery

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Independent	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Epidural analgesia	0.463	0.785 (0.412–1.497)	0.338	0.688 (0.320–1.479)
General information				
Age (years)	0.613	1.020 (0.945–1.101)	0.574	1.025 (0.940–1.119)
Gestational age at delivery (weeks)	0.053	0.831 (0.689–1.003)		
BMI (kg/m^2)	0.393	0.959 (0.871–1.056)	0.196	0.929 (0.830–1.039)
Gravidity (Primipara vs multipara)	0.790	0.916 (0.481–1.744)		
Maternal education > 12 y	0.689	0.861 (0.415–1.788)		
Husband education > 12 y	0.335	0.695 (0.332–1.456)		
Occupation				
Office worker		1.000 (Ref)		
Professional/business	0.531	1.431 (0.467–4.386)		
Service	0.767	0.837 (0.257–2.722)		
Self-employed	0.525	0.604 (0.128–2.861)		
Migrant worker	0.903	0.906 (0.185–4.440)		

OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; ¥: Chinese Yuan. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 13.304, df = 8, p = 0.102. Cox and Snell pseudo-R^2 = 0.137. Nagelkerke pseudo-R^2 = 0.228.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Housewife	0.590	1.359 (0.445–4.148)		
Others	0.247	1.661 (0.703–3.928)		
Family income (¥/mo)				
≤ 3,000		1.000 (Ref)		
3000–6,000	0.931	1.111 (0.103–11.965)		
6000–10000	0.466	0.419 (0.040–4.356)		
10000–20000	0.757	0.692 (0.067–7.128)		
> 20000	0.644	0.568 (0.051–6.275)		
Impact of childbirth on work or re-employment	0.996	1.003 (0.390–2.578)		
Remarried	0.841	0.803 (0.094–6.837)		
History of abnormal pregnancy	0.950	0.978 (0.482–1.983)		
Pregnancy with obstetric disease	0.431	0.606 (0.174–2.110)		
Maternity leave time				
None		1.000 (Ref)		1.000 (Ref)
Legal time	0.146	2.491 (0.729–8.514)	0.097	3.087 (0.816–11.680)
Full time	0.038	11.333 (1.150-111.692)	0.161	5.590 (0.503–62.165)
Anxiety and depression during pregnancy	0.006	4.278 (1.502–12.181)	0.169	2.276 (0.704–7.353)

OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; ¥: Chinese Yuan. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 13.304, df = 8, p = 0.102. Cox and Snell pseudo-R^2 = 0.137. Nagelkerke pseudo-R^2 = 0.228.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
History of depression and trauma		NA		
Cigarette, alcohol, and long-term medication use		NA		
Husband's satisfaction with infant's sex	0.262	0.203 (0.012–3.303)		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.195	0.300 (0.049–1.850)		
Maternity classes	0.985	0.993 (0.470–2.095)		
Internet resources or books	0.923	0.926 (0.193–4.437)		
Unplanned pregnancy	0.010	2.426 (1.231–4.779)	0.113	1.905 (0.859–4.223)
Parturient is only child	0.757	0.862 (0.338–2.199)		
Changes in marital relationship during pregnancy	0.863	1.216 (0.133–11.142)		
Method of GDM control (diet vs. medication)	0.952	0.966 (0.314–2.975)		
Maternal blood glucose control during pregnancy (abnormal vs. normal)	0.003	0.326 (0.155–0.688)	0.144	0.534 (0.230–1.240)
SAS score	< 0.001	1.096 (1.047 -1.146)	0.003	1.078 (1.023–1.132)
SSRS score	0.006	0.949 (0.914–0.985)	0.026	0.952 (0.911–0.994)
Mode of delivery (Cesarean vs. vaginal birth)		NA		
Neonatal weight ≥ 3500 g	0.626	0.827 (0.384–1.777)		
NICU admission after birth	0.599	1.257 (0.536–2.944)		

OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; ¥: Chinese Yuan. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 13.304, df = 8, p = 0.102. Cox and Snell pseudo-R^2 = 0.137. Nagelkerke pseudo-R^2 = 0.228.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)
NICU admission after birth for hypoglycemia treatment	0.923	1.080 (0.225–5.176)	

OR: odds ratio; 95% CI: 95% confidence interval; BMI: body mass index; SAS: Self-Rating Anxiety Scale; SSRS: Social Support Rating Scale; ¥: Chinese Yuan. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 13.304$, df = 8, p = 0.102. Cox and Snell pseudo-$R^2 = 0.137$. Nagelkerke pseudo-$R^2 = 0.228$.

In addition, propensity score matching was performed to reduce the potential selection bias and verify the results of the univariate and multivariate analyses with “epidural analgesia” as the dependent variable and the other factors as the independent variables. The variables that showed a statistically significant difference between the two groups were then taken as the independent variables (age, gravidity, occupation, history of adverse pregnancy outcomes, and SSRS score). The 1:1 nearest neighbor matching method was used, and the caliper value was set to 0.02. A total of 69 fuzzy matching pairs were obtained. Logistic regression analysis was performed after matching. On univariate analysis, PPD at 24 h after delivery was considered the dependent variable and “epidural analgesia” and “other confounding factors” as independent variables. Then the factors for which $p < 0.05$ were included in the multivariate model, and stepwise regression was performed according to the Akaike information criterion minimum standard (Table 5). From this analysis, three independent factors were identified: epidural analgesia (protective factor), unplanned pregnancy (risk factor), and SAS score (risk factor). Epidural analgesia was a protective factor against PPD at 24 h after delivery (odds ratio [OR], 0.301; 95% confidence interval [CI], 0.104–0.867; $p < 0.05$).

Table 5
Results of univariate and multivariate analyses of factors associated with PPD at 24 h after delivery after propensity score matching.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Independent	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Epidural analgesia	0.058	0.425 (0.176–1.028)	0.026	0.301 (0.104–0.867)
General information				
Age (years)	0.384	0.953 (0.856–1.061)	0.707	0.977 (0.865–1.103)
Gestational age at delivery (weeks)	0.037	0.772 (0.605–0.984)	0.076	0.753 (0.550–1.031)
BMI (kg/m^2)	0.399	0.953 (0.852–1.066)	0.346	0.940 (0.826–1.069)
Gravidity (Primipara vs multipara)	0.749	1.150 (0.489–2.701)		
Maternal education > 12 y	0.571	0.763 (0.300-1.941)		
Husband education > 12 y	0.225	0.554 (0.214–1.437)		
Occupation				
Office worker		1.000 (Ref)		
Professional/business	1.000	1.000 (0.187–5.357)		
Service	0.782	1.227 (0.288–5.226)		
Self-employed	0.417	0.409 (0.047–3.543)		

Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 7.083$, df = 8, $p = 0.528$. Cox and Snell pseudo-R^2 = 0.199. Nagelkerke pseudo-R^2 = 0.316.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)
Migrant worker	0.892	1.125 (0.207–6.123)	
Housewife	0.959	1.038 (0.248–4.340)	
Others	0.274	1.929 (0.595–6.254)	
Family income (¥/mo)			
≤ 3,000		1.000 (Ref)	
3000–6,000	0.671	0.533 (0.029–9.708)	
6000–10000	0.288	0.211 (0.012–3.731)	
10000–20000	0.213	0.158 (0.009–2.877)	
> 20000	0.305	0.211 (0.011–4.121)	
Impact of childbirth on work or re-employment	0.832	0.866 (0.230–3.257)	
Remarried	0.782	1.385 (0.138–13.856)	
History of abnormal pregnancy	0.390	0.647 (0.240–1.747)	
Pregnancy with obstetric disease		NA	
Maternity leave time			
None		1.000 (Ref)	

Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 7.083$, df = 8, $p = 0.528$. Cox and Snell pseudo-R^2 = 0.199. Nagelkerke pseudo-R^2 = 0.316.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Legal time	0.812	1.212 (0.249–5.898)		
Full time	0.527	2.500 (0.146–42.800)		
Anxiety and depression during pregnancy	0.039	4.652 (1.083–19.978)		
History of depression and trauma		NA		
Cigarette, alcohol, and long-term medication use		NA		
Husband's satisfaction with infant's sex		NA		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.782	0.722 (0.072–7.227)		
Maternity classes	0.225	0.554 (0.214–1.437)		
Internet resources or books	0.855	1.226 (0.137–10.952)		
Unplanned pregnancy	0.001	4.496 (1.824–11.082)	0.008	4.207 (1.461–12.111)
Parturient is only child	0.962	0.974 (0.330–2.871)		
Changes in marital relationship during pregnancy	0.552	2.096 (0.183–24.008)		
Method of GDM control (diet vs. medication)	0.505	1.609 (0.397–6.522)		

Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 7.083$, df = 8, $p = 0.528$. Cox and Snell pseudo-R^2 = 0.199. Nagelkerke pseudo-R^2 = 0.316.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Maternal blood glucose control during pregnancy (abnormal vs. normal)	0.011	0.261 (0.093–0.735)	0.066	0.319 (0.094–1.080)
SAS score	0.004	1.089 (1.027–1.154)	0.034	1.073 (1.006–1.146)
SSRS score	0.557	0.986 (0.939–1.035)	0.999	1.000 (0.943–1.060)
Mode of delivery (Cesarean vs. vaginal birth)		NA		
Neonatal weight ≥ 3500 g	0.835	0.903 (0.347–2.348)		
NICU admission after birth	0.774	0.842 (0.261–2.716)		
NICU admission after birth for hypoglycemia treatment	0.441	0.436 (0.053–3.597)		

Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 7.083$, df = 8, $p = 0.528$. Cox and Snell pseudo-R^2 = 0.199. Nagelkerke pseudo-R^2 = 0.316.

Only the SAS score was a common independent influencing factor on PPD at 24 h post-delivery in the GDM population before and after propensity matching (Fig. 2).

When set PPD at 42 days post-delivery was applied as a dependent variable, four significant factors among all of the parturient and neonatal variables were identified on univariate analysis ($p < 0.05$): anxiety and depression during pregnancy, history of depression and trauma, unplanned pregnancy, and SAS score. Of these, multivariate logistic regression analysis then identified two factors independently associated with PPD: anxiety and depression during pregnancy and unplanned pregnancy (Table 6).

Table 6
Results of univariate and multivariate analyses of factors associated with PPD at 42 days after delivery

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Independent	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Epidural analgesia	0.191	1.602 (0.791–3.247)	0.126	1.878 (0.837–4.214)
General information				
Age (years)	0.589	0.977 (0.897–1.063)	0.790	1.013 (0.922–1.113)
Gestational age at delivery (weeks)	0.647	0.951 (0.765–1.181)		
BMI (kg/m^2)	0.854	0.991 (0.895–1.096)	0.647	0.973 (0.866–1.093)
Gravidity (Primipara vs multipara)	0.393	0.738 (0.368–1.481)		
Maternal education > 12 y	0.411	0.724 (0.336–1.563)		
Husband education > 12 y	0.627	0.817 (0.361–1.849)		
Occupation				
Office worker		1.000 (Ref)		
Professional/business	0.489	0.578 (0.122–2.732)		
Service	0.971	0.978 (0.296–3.228)		
Self-employed	0.867	1.122 (0.291–4.330)		
Migrant worker	0.944	1.060 (0.214–5.245)		
Housewife	0.833	0.867 (0.229–3.282)		

Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 5.181, df = 8, p = 0.738. Cox and Snell pseudo-R^2 = 0.084. Nagelkerke pseudo-R^2 = 0.152.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Others	0.383	1.506 (0.600-3.776)		
Family income (¥/mo)				
≤ 3,000		1.000 (Ref)		
3000–6,000	0.545	0.469 (0.040–5.441)		
6000–10000	0.323	0.303 (0.029–3.228)		
10000–20000	0.704	0.636 (0.062–6.577)		
> 20000	0.739	0.667 (0.061–7.271)		
Impact of childbirth on work or re-employment	0.322	0.535 (0.155–1.845)		
Remarried	0.987	1.019 (0.119–8.710)		
History of abnormal pregnancy	0.746	0.879 (0.403–1.917)		
Pregnancy with obstetric disease	0.839	1.124 (0.364–3.469)		
Maternity leave time				
None		1.000 (Ref)		
Legal time	0.280	1.979 (0.574–6.818)		
Full time	0.307	3.778 (0.294–48.505)		
Anxiety and depression during pregnancy	0.001	5.626 (1.9551–16.221)	0.006	4.880 (1.568–15.193)
History of depression and trauma	0.039	12.857 (1.136-145.566)	0.059	11.163 (0.916-136.075)
Cigarette, alcohol, and long-term medication use		NA		

Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 5.181, df = 8, p = 0.738. Cox and Snell pseudo-R^2 = 0.084. Nagelkerke pseudo-R^2 = 0.152.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Husband's satisfaction with infant's sex		NA		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.120	0.235 (0.038–1.459)		
Maternity classes	0.411	0.724 (0.336–1.563)		
Internet resources or books	0.690	0.726 (0.151-3.500)		
Unplanned pregnancy	0.006	2.752 (1.335–5.673)	0.030	2.404 (1.090–5.305)
Parturient is only child	0.808	0.882 (0.321–2.424)		
Changes in marital relationship during pregnancy		NA		
Method of GDM control (diet vs. medication)	0.817	0.861 (0.244–3.046)		
Maternal blood glucose control during pregnancy (abnormal vs. normal)	0.139	0.532 (0.230–1.228)		
SAS score	0.035	1.050 (1.003–1.099)	0.215	1.031 (0.982–1.082)
SSRS score	0.364	0.981 (0.942–1.022)	0.896	0.997 (0.852–1.044)
Mode of delivery (Cesarean vs. vaginal birth)	0.199	6.250 (0.382-102.169)		
NICU admission after birth	0.854	1.093 (0.424–2.818)		
NICU admission after birth for hypoglycemia treatment	0.631	0.600 (0.075–4.830)		
Chronic pain within 42 days	0.459	1.415 (0.573–3.492)		
42-day maternal blood glucose				
Normal		1.000 (Ref)		

Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 5.181, df = 8, p = 0.738. Cox and Snell pseudo-R^2 = 0.084. Nagelkerke pseudo-R^2 = 0.152.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)
High	0.766	0.793 (0.172–3.653)	
Not tested	0.120	1.819 (0.855–3.870)	
Feeding patterns			
Breastfeeding		1.000 (Ref)	
Lactancia artificia	0.941	0.972 (0.457–2.065)	
Mixed Feeding	0.642	0.696 (0.151–3.214)	
Living with parent-in-law	0.729	1.144 (0.533–2.456)	
Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 5.181, df = 8, p = 0.738. Cox and Snell pseudo-R^2 = 0.084. Nagelkerke pseudo-R^2 = 0.152.			

In addition, propensity score matching was applied again as described above to reduce the potential selection bias and verify the results. For univariate analysis, PPD at 42 days after delivery as the dependent variable and “epidural analgesia” and “other confounding factors” as independent variables. Then the factors for which $p < 0.05$ were included in the multivariate model, which identified two independent risk factors for PPD at 42 days post-delivery: anxiety and depression during pregnancy and unplanned pregnancy (Table 7).

Table 7
Results of univariate and multivariate analyses of factors associated with PPD at 42 days after delivery after propensity score matching

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Independent	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Epidural analgesia	0.642	1.242 (0.498-3.100)	0.630	1.295 (0.473–3.549)
General information				
Age (years)	0.393	0.950 (0.845–1.068)	0.316	0.934 (0.818–1.067)
Gestational age at delivery (weeks)	0.661	0.945 (0.734–1.217)		
BMI (kg/m^2)	0.682	0.975 (0.866–1.099)	0.976	0.982 (0.859–1.124)
Gravidity (Primipara vs multipara)	0.838	0.909 (0.364–2.272)		
Maternal education > 12 y	0.450	0.682 (0.253–1.840)		
Husband education > 12 y	0.830	0.887 (0.297–2.648)		
Occupation				
Office worker		1.000 (Ref)		
Professional/business		NA		
Service	0.850	0.852 (0.162–4.474)		
Self-employed	0.483	1.704 (0.384–7.553)		

Data were matched by propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 6.441, df = 8, p = 0.598. Cox and Snell pseudo-R^2 = 0.116. Nagelkerke pseudo-R^2 = 0.199.

Variable	Univariate analysis (n = 138)	Multivariate analysis (n = 138)
Migrant worker	0.612	0.568 (0.064–5.054)
Housewife	0.823	1.179 (0.278-5.000)
Others	0.713	1.278 (0.345–4.726)
Family income (¥/mo)		
≤ 3,000		1.000 (Ref)
3000–6,000	0.394	0.278 (0.015–5.273)
6000–10000	0.158	0.122 (0.007–2.268)
10000–20000	0.169	0.128 (0.007–2.387)
> 20000	0.485	0.353 (0.019–6.569)
Impact of childbirth on work or re-employment	0.252	0.298 (0.037–2.369)
Remarried	0.620	1.794 (0.178–18.081)
History of abnormal pregnancy	0.482	0.681 (0.233–1.990)
Pregnancy with obstetric disease		NA
Maternity leave time		
None		1.000 (Ref)

Data were matched by propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 6.441$, df = 8, p = 0.598. Cox and Snell pseudo-$R^2 = 0.116$. Nagelkerke pseudo-$R^2 = 0.199$.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Legal time	0.479	2.136 (0.261–17.484)		
Full time	0.290	5.500 (0.235-128.968)		
Anxiety and depression during pregnancy	0.015	6.222 (1.427–27.131)	0.027	6.197 (1.233–31.149)
History of depression and trauma		NA		
Cigarette, alcohol, and long-term medication use		NA		
Husband's satisfaction with infant's sex		NA		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.620	0.558 (0.055–5.620)		
Maternity classes	0.830	0.887 (0.297–2.648)		
Internet resources or books	0.960	0.946 (0.105–8.513)		
Unplanned pregnancy	0.002	4.524 (1.732–11.816)	0.003	4.837 (1.695–13.801)
Parturient is only child	0.931	0.949 (0.292–3.086)		
Changes in marital relationship during pregnancy		NA		
Method of GDM control (diet vs. medication)	0.833	1.189 (0.239–5.917)		
Maternal blood glucose control during pregnancy (abnormal vs. normal)	0.514	0.668 (0.199–2.245)		

Data were matched by propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 6.441$, df = 8, p = 0.598. Cox and Snell pseudo-$R^2 = 0.116$. Nagelkerke pseudo-$R^2 = 0.199$.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
SAS score	0.173	1.041 (0.982–1.104)	0.714	1.012 (0.949–1.080)
SSRS score	0.559	1.016 (0.962–1.074)	0.232	1.040 (0.975–1.109)
Mode of delivery (Cesarean vs. vaginal birth)		NA		
Neonatal weight ≥ 3500 g	0.624	1.280 (0.477–3.433)		
NICU admission after birth	0.678	0.758 (0.205–2.807)		
NICU admission after birth for hypoglycemia treatment		NA		
Chronic pain within 42 days	0.984	0.987 (0.262–3.720)		
42-day maternal blood glucose				
Normal		1.000 (Ref)		
High	0.865	1.152 (0.227–5.848)		
Not tested	0.270	1.747 (0.648–4.710)		
Feeding patterns				
Breastfeeding		1.000 (Ref)		
Lactancia artificia	0.624	1.278 (0.479–3.409)		
Mixed Feeding	0.957	1.045 (0.206–5.318)		

Data were matched by propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; $\chi^2 = 6.441$, df = 8, p = 0.598. Cox and Snell pseudo-$R^2 = 0.116$. Nagelkerke pseudo-$R^2 = 0.199$.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)
Living with parent-in-law	0.822	1.125 (0.402–3.145)	
Data were matched by propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 6.441, df = 8, p = 0.598. Cox and Snell pseudo-R^2 = 0.116. Nagelkerke pseudo-R^2 = 0.199.			

Anxiety and depression during pregnancy as well as unplanned pregnancy were the common independent influencing factors for PPD at 42 days post-delivery in our GDM population before and after propensity matching (Fig. 3).

Models for predicting PPD at 24 h and 42 days after delivery in parturients with GDM

Two factors identified on multiple logistic regression analysis as significantly associated with PPD at 24 h were used in a model, and the ability of that model to predict PPD at 24 h after delivery in parturients with GDM was tested by receiver operating characteristic (ROC) curve analysis. The model without propensity score matching showed an area under the curve (AUC) value of 0.748 (95% CI: 0.660–0.835) when $p < 0.001$ was selected as the best diagnosis point, with a sensitivity of 0.578, specificity of 0.844, positive predictive value of 0.433, and negative predictive value of 0.906. With propensity score matching, the model showed an AUC value of 0.806 (95% CI: 0.718–0.895) when $p < 0.001$ was selected as the best diagnosis point, with a sensitivity of 0.815, specificity of 0.694, positive predictive value of 0.393, and negative predictive value of 0.939 (Fig. 4).

The factors identified by multiple logistic regression as significantly associated with PPD at 42 days after delivery in parturients with GDM were also combined in a model, and the ability of the model to predict PPD at 42 days post-delivery in these patients was tested. The model without propensity score matching showed an AUC value of 0.716 (95% CI: 0.620–0.812) when $p < 0.001$ was selected as the best diagnosis point, with a sensitivity of 0.595, specificity of 0.770, positive predictive value of 0.297, and negative predictive value of 0.921. The model with propensity score matching showed an AUC of 0.772 (95% CI: 0.655–0.890), with a sensitivity of 0.818, specificity of 0.690, positive predictive value of 0.333, and negative predictive value of 0.952 (Fig. 5).

Factors associated with neonate transfer to the NICU for hypoglycemia treatment

To further analyze the influence of epidural labor analgesia on the health of the newborn, we considered the rate of neonatal hypoglycemia requiring further treatment in the NICU as the risk index of neonatal hypoglycemia and regarded it as the dependent variable in univariate and multivariate analyses. Univariate logistic regression analysis identified two maternal and infant variables as significantly

associated with the rate of neonatal hypoglycemia ($p < 0.05$): epidural analgesia and method of diabetes control (diet vs. medication). Multivariate logistic regression analysis further identified only one independent predictor, method of diabetes control (diet vs. medication) as a risk factor (OR, 5.277; 95% CI, 1.181–23.580; $p < 0.05$) that increased the risk of neonate transfer to the NICU for hypoglycemia treatment (Table 8).

Table 8
Results of univariate and multivariate analyses of factors associated with the rate of neonate transfer to the NICU for hypoglycemia treatment

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)	
Independent	p	OR (95% CI)	p	OR (95% CI)
Epidural analgesia	0.046	4.872 (1.032–22.999)	0.072	4.478 (0.877–22.874)
General information				
Age (years)	0.136	0.887 (0.757–1.039)	0.191	0.890 (0.747–1.060)
Gestational age at delivery (weeks)	0.171	1.588 (0.819–3.079)		
BMI (kg/m^2)	0.218	1.102 (0.944–1.287)	0.168	1.145 (0.944–1.389)
History of abnormal pregnancy	0.881	0.902 (0.233–3.495)		
Pregnancy with obstetric disease	0.928	0.908 (0.112–7.391)		
Anxiety and depression during pregnancy	0.109	3.778 (0.744–19.170)		
History of depression and trauma		NA		
Cigarette, alcohol, and long-term medication use		NA		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.117	0.161 (0.016–1.578)		
Maternity classes	0.108	0.367 (0.108–1.245)		
Internet resources or books	0.421	0.413 (0.048–3.550)		
Unplanned pregnancy	0.841	1.149 (0.296–4.466)		
Method of diabetes control (diet vs. medication)	0.047	4.125 (1.017–16.729)	0.029	5.277 (1.181–23.580)

Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 9.812, df = 8, p = 0.278. Cox and Snell pseudo-R^2 = 0.045. Nagelkerke pseudo-R^2 = 0.153.

Variable	Univariate analysis (n = 263)		Multivariate analysis (n = 263)
Maternal blood glucose control during pregnancy	0.838	0.849 (0.177–4.077)	
Mode of delivery (Cesarean vs. vaginal birth)		NA	
Neonatal weight ≥ 3500 g	0.865	1.125 (0.290–4.371)	
Duration of labor (min)			
Stage 1	0.076	1.001 (1.000-1.003)	
Stage 2	0.583	0.995 (0.976–1.014)	
Stage 3	0.581	1.024 (0.942–1.113)	
Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 9.812, df = 8, p = 0.278. Cox and Snell pseudo-R^2 = 0.045. Nagelkerke pseudo-R^2 = 0.153.			

We then repeated the univariate and multivariate analyses for factors influencing the rate of neonate transfer to the NICU for hypoglycemia treatment after propensity score matching, using the same independent variables and parameters as described above (Table 9). From this multivariate analysis, only epidural analgesia was identified as a risk factor for neonatal hypoglycemia (OR, 12.526, 95% CI, 1.322–117.776; $p < 0.05$).

Table 9
Results of univariate and multivariate analyses of factors influencing the rate of neonate transfer to the NICU for hypoglycemia treatment after propensity score matching

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Independent	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Epidural analgesia	0.030	10.200 (1.255–82.875)	0.027	12.526 (1.332-117.776)
General information				
Age (years)	0.256	0.903 (0.757–1.077)	0.160	0.873 (0.722–1.055)
Gestational age at delivery (weeks)	0.128	1.729 (0.855–3.494)		
BMI (kg/m^2)	0.188	1.106 (0.952–1.284)	0.104	1.202 (0.963–1.501)
History of abnormal pregnancy	0.520	0.592 (0.120–2.919)		
Pregnancy with obstetric disease	0.948	1.074 (0.125–9.219)		
Anxiety and depression during pregnancy	0.561	1.921 (0.212–17.369)		
History of depression and trauma		NA		
Cigarette, alcohol, and long-term medication use		NA		
Source of health knowledge during pregnancy				
Routine obstetric examination	0.204	0.216 (0.020–2.292)		
Maternity classes	0.139	0.364 (0.095–1.388)		
Internet resources or books		NA		
Unplanned pregnancy	0.804	0.817 (0.164–4.055)		
Method of diabetes control (diet vs. medication)	0.556	0.613 (0.120–3.131)		

Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 9.992, df = 8, p = 0.266. McFadden's pseudo-R^2 = 0.229. Cox and Snell pseudo-R^2 = 0.109. Nagelkerke pseudo-R^2 = 0.269.

Variable	Univariate analysis (n = 138)		Multivariate analysis (n = 138)	
Maternal blood glucose control during pregnancy	0.017	6.429 (1.392–29.694)	0.053	5.384 (0.976–29.714)
Mode of delivery (Cesarean vs. vaginal birth)		NA		
Neonatal weight ≥ 3500 g	0.856	1.139 (0.279–4.652)		
Duration of labor (min)				
Stage 1	0.053	1.002 (1.000-1.003)		
Stage 2	0.638	0.996 (0.977–1.014)		
Stage 3	0.352	1.045 (0.953–1.146)		
Data were matched by using propensity score matching with 1:1 nearest neighbor matching. Hosmer and Lemeshow goodness of fit (GOF) test; χ^2 = 9.992, df = 8, p = 0.266. McFadden's pseudo-R^2 = 0.229. Cox and Snell pseudo-R^2 = 0.109. Nagelkerke pseudo-R^2 = 0.269.				

Thus, each analysis, with or without propensity score matching, identified one independent factor influencing the rate of neonate transfer to the NICU for hypoglycemia treatment was identified among parturients with GDM, but the factors differed with and without propensity score matching (method of diabetes control without propensity score matching and epidural labor analgesia with propensity score matching; Fig. 6).

Model for predicting neonate transfer to the NICU for hypoglycemia treatment after delivery by parturients with GDM

Two models based on the results of multiple logistic regression analysis were tested for their ability to predict the rate of neonate transfer to the NICU for hypoglycemia treatment. The model without propensity score matching showed an AUC value of 0.749 (95% CI: 0.567–0.930), with a sensitivity of 0.545, specificity of 0.925, positive predictive value of 0.240, and negative predictive value of 0.979. The model with propensity score matching showed an AUC value of 0.822 (95% CI: 0.672–0.972), with a sensitivity of 0.700, specificity of 0.852, positive predictive value of 0.240, and negative predictive value of 0.965 (Fig. 7).

Discussion

The causes of PPD are complex, with many possible influencing factors [44, 45]. Early labor pain intensity is known to be associated with emotional disorder, and early postpartum labor pain is associated with

PPD [26, 27]. Furthermore, severe pain during delivery may be related to the patient's psychological reaction, and the influence of emotional state on pain experience has been widely recognized [46]. An adverse psychological state of parturients is closely related to the occurrence of PPD, and labor pain is recognized as an important cause of adverse emotions during childbirth [30]. In the present study, labor pain was assessed at three time points, and as expected, the pain scores (NRS scores) of patients who received epidural analgesia were significantly lower than those in the control group (Table 2). Several studies have reported that epidural labor analgesia may decrease the incidence of PPD [16, 26, 28, 30], with two of these studies finding a positive correlation between labor pain score and the early postpartum EPDS score [26, 30]. Boudou et al [26] reported a significant positive correlation between labor pain and the EPDS score specifically at 3 days postpartum, while Hiltunen et al [30] reported that pain relief during vaginal delivery decreased the risk of PPD, especially immediately after delivery. Ding et al [16] reported that epidural labor analgesia decreased the incidence of PPD at 42 days after delivery. The increased emotional response to anticipated pain is known to impair the ability to regulate pain, and the brain neural network activated during the experience of psychological pain overlaps with the brain regions involved in physical pain [47]. In parturients suffering from pain and/or major depression, the ability to respond to emotional information is impaired [48]. However, other studies found no relationship between epidural analgesia and PPD [9, 12, 49–52], and currently, the American College of Obstetrics and Gynecology (ACOG) and the United States Preventive Services Task Force do not regard labor pain as a risk factor for PPD [42, 51]. In addition to labor pain, other factors that have been found to be independently associated with PPD include: prenatal depression, self-esteem, childcare stress, prenatal anxiety, life stress, social support, marital relationship, history of previous depression, infant temperament, maternity blues, marital status, socioeconomic status, and unplanned/unwanted pregnancy [53]. Thus, additional studies are needed to clarify the relationship between epidural labor analgesia and PPD in the general population of pregnant mothers and in those with specific conditions, such as GDM.

Previous research has also implicated GDM as a potential risk factor of PPD. In a study of 1801 women in Iran, Abdollahi et al [54] found a significant correlation between GDM and PPD (OR = 2.93, 95% CI, 1.46–5.88). The United States Preventive Services Task Force also lists GDM as a risk factor for PPD [55]. GDM creates a background of changes in metabolic status, the inflammatory state, and the hypothalamus-pituitary-adrenal axis that are associated with an increased risk of depression.[34–36] However, in the study of Miller et al [56], the relationship between GDM and PPD was not significant. The reported rates of PPD in the general maternal population are within the range of11–19.2% (13%) [13, 14], and in the parturients with GDM in the present study, the incidence rates of PPD (11.28–18.8%) were not higher than this normal range. However, our multivariate analysis after propensity score matching for variable that differed between our epidural and control groups did identify epidural labor analgesia as a protective factor for PPD at 24 h post-delivery (OR, 0.301, 95% CI: 0.104–0.867; $p < 0.05$). In our analysis, the significant independent variables were age, gravidity, history of abnormal pregnancy, occupation, and SSRS. We applied these variables as independent variables, used the 1:1 nearest neighbor matching

method, and conducted the logistic regression analysis after propensity score matching to reduce potential selection bias.

In the present study, SAS score and unplanned pregnancy were also found to be risk factors of PPD at 24 h after delivery in parturients with GDM, while anxiety and depression during pregnancy and unplanned pregnancy were risk factors for PPD at 42 days post-delivery in our patients. It is well known that the physiological and psychological changes during pregnancy are likely to induce anxiety and other emotional problems during childbirth. Anxiety is a normal cognitive activity and emotional response, but excessive anxiety can increase the risk of mental illness [57]. A retrospective study of 2926 male and 1929 female adult twins [58] showed that anxiety is the primary risk factor for major depressive disorder (MDD). Previous research has also found that perinatal anxiety and depression are important risk factors of PPD [59–61]. Heron et al [62] suggested that antenatal anxiety might predict PPD at 8 weeks and 8 months after delivery. The SAS is commonly used to evaluate the anxiety state of parturients before and after delivery, as it reflects internalized factors [63], and the SSRS is often used to assess women's social support [64]. In the present study, a high SAS score was a risk factor for PPD, and a high SSRS score was a protective factor against PPD, which is consistent with conclusions in the existing literature [53, 65]. Positive social support is one of the most effective means to overcoming stress and has been correlated with the relief of depression and anxiety disorder [66].

Unplanned pregnancy has also been shown to be a risk factor for PPD in general populations,[67–69] and studies have found that approximately half of pregnancies are unplanned.[65, 66] A multicenter study of 290 Japanese women [67] showed that women with an unplanned pregnancy had a higher incidence of severe depression during pregnancy and of PPD at 3 months after delivery. Another study [68] of 2076 South Korean women showed that the risk of depression was increased by 20–22% for an unplanned pregnancy. Another prospective study of 688 women in the United States found that unplanned pregnancy was a risk factor for PPD at 3 and 12 months after delivery [69]. In the present study of parturients with GDM, our results indicate that unplanned pregnancy was a risk factor for PPD at 24 h and 42 days after delivery, consistent with the literature described above [67–69]. These findings have important implications for future research and women's pregnancy care, as women with unplanned pregnancy should be regarded as an at-risk population for early detection and prevention of PPD [70].

In the present study, epidural labor analgesia significantly prolonged the first and second stages of labor, but the durations of these stages were still within the normal ranges (Table 2), as experts have concluded that the upper limit for the second stage delivery should be 4 h for primiparas with epidural analgesia and 3 h for primiparas without epidural analgesia [71]. Previous studies have also reported that epidural labor analgesia can prolong the first and second stages of labor [22, 72–74], which is consistent with our results. Inconsistently though, two studies [22, 75] reported that epidural administration of 0.08% ropivacaine and 0.4 μg/ml sufentanil did not prolong the second stage of labor. This discrepancy may be related to the use of different local anesthetic concentrations (0.1% ropivacaine and 0.4 μg/ml sufentanil in the present study). In this study, the incidence rates of pruritus, dizziness, and urine retention were higher in the epidural group than in the control group, which may be related to the epidural administration

of opioids [39, 41]. Every treatment has advantages and disadvantages, and indeed, epidural analgesia can induce side effects while reducing labor pain. Importantly, in this study, epidural labor analgesia did not increase the percentage of patients who required delivery by cesarean section. The vaginal delivery rate in the epidural group was still similar to that in the control group, which is encouraging. Thus, although epidural analgesia may have prolonged the first and second stages of labor and induced mild side effects, the delivery outcome was not affected. Furthermore, from our logistic regression analysis, the duration of the labor stage was not associated with an increased risk of PPD.

Diabetes control with medication and epidural analgesia were both identified as risk factors for neonate transfer to the NICU for hypoglycemia treatment among our GDM population. In women with GDM, diet is the first choice for blood glucose control, but if the effect is insufficient, drug control is the better choice. This means that women who require drug control are more likely to have experienced poor blood glucose control. Blachier et al [76] found that neonatal hypoglycemia is associated with drug control of GDM and not associated with diet control of GDM, which is consistent with our results.

The pain and tension experienced during the perinatal period lead to a significant increase in the blood glucose concentration [77], and the fetal plasma catecholamine level can reach a very high level during delivery. This increase can be avoided by appropriate maternal pain relief and sympathetic block after epidural anesthesia [78]. Indeed, epidural anesthesia reduces maternal stress hormone levels during labor [8]. Studies have found that 6 h after delivery, the plasma cortisol level of parturients who received epidural anesthesia is lower than that in those who did not receive epidural anesthesia [9]. This study found that the incidence of hypoglycemia in newborns at 2 h and 3 h after birth as well as the proportion of neonates with hypoglycemia requiring NICU treatment were higher in the epidural group than in the control group. These differences may be due to the fact that labor analgesia inhibits the stress response induced by pain and tension. If the concentration of catecholamine is significantly reduced, the increase in blood glucose concentration may also be inhibited [79]. Another study showed that during childbirth, the serum concentrations of cortisol and adrenaline of mothers abruptly decreased, which could trigger an acute hypoglycemic event [80]. With the onset of pain relief, the catecholamine concentration decreases significantly, potentially resulting in an acute hypoglycemia attack in a diabetic parturient after administration of labor analgesia [37]. Our results showed that the incidence of postpartum newborn hypoglycemia (< 47 mg/dl [2.6 mmol/l]) was 11.54% in the epidural group and 6.02% in the control group. A cohort study in an Israeli medical center reported an incidence of neonatal hypoglycemia of 12.1% among all newborns at 74 min after delivery [81]. The lower rates in our study population may be due to differences in the subjects and deliveries. Overall, epidural analgesia is known to potentially lead to maternal hypoglycemia, which then leads to neonatal hypoglycemia. Because repeated or persistent severe hypoglycemia may cause damage to the central nervous system [75], it is necessary to monitor neonatal blood glucose levels closely after administration of epidural analgesia and apply timely treatment for neonatal hypoglycemia.

The optimal timing of PPD assessment has been controversial. One study found that when commonly used depression rating scales were administered to identify PPD immediately after delivery, their

psychometric properties were not satisfactory [82]. Although depression symptoms immediately after delivery are frequent but transient, application of the EPDS subscale immediately after delivery provides insight into a spectrum of postpartum psychological problems, which are associated with later depressive disorders [40]. In the present study, the EPDS score was assessed at 24 h after delivery and then again at 42 days after delivery. The EPDS score at 42 days was used for preliminary screening for diagnosis of PPD. Our analysis did reveal a significant correlation between the EPDS score at 24 h post-delivery and that at 42 days after delivery (Pearson correlation coefficient = 0.527, $p < 0.001$).

This study has several limitations that should be considered. First, continuous monitoring of the blood glucose concentration of parturients was lacking, as invasive blood glucose monitoring was rejected by the patients and not strictly enforced. Second, group allocation was determined according to maternal choice. Third, the presence of depression was not assessed before delivery. Fourth, PPD was not diagnosed by psychiatrists; however, the EPDS is an established tool for the detection of PPD by non-psychiatrists [83, 84] and has been well verified in China [85]. Lastly, the follow-up time was short at only 42 days.

Several advantages of the present study are also worth noting. To our knowledge, this was the first study to investigate the effects of epidural analgesia in pregnant women with GDM and their newborns. The sample size was 263, which is larger than the samples sizes of relevant previous studies [16, 86]. We also retained 86.5% of the study participants at the final follow-up. Although we found that epidural analgesia could prolong the first and second stages of labor and increase the incidence rates of maternal side effects and neonatal hypoglycemia, its clinical benefit (reducing labor pain) was still clear. More research is needed to understand the association between epidural analgesia and hypoglycemia of neonates born to parturients with GDM, as this study identifies such an association for the first time. Additionally, more research on the optimal drug combination and dosage for epidural labor analgesia is needed in the future to improve pain relief while reducing the incidence of side effects.

Epidural labor analgesia may be a protective factor against PPD but a risk factor for neonatal hypoglycemia. Further studies with a larger sample size and longer follow-up time are needed to better characterize the effect of epidural labor analgesia on PPD and neonatal hypoglycemia.

Conclusion

Epidural labor analgesia may be a protective factor against PPD but a risk factor for neonatal hypoglycemia. Further studies with a larger sample size and longer follow-up time are needed to better characterize the effect of epidural labor analgesia on PPD and neonatal hypoglycemia.

Abbreviations

PPD, Postpartum depression; GDM, Gestational diabetes mellitus; EPDS, Edinburgh Postnatal Depression Scale; BMI, Body mass index; OGTT, Oral glucose tolerance test; NRS, Numerical Rating Scale;

PCEA, Patient-controlled epidural analgesia; NICU, Neonatal intensive care unit; SAS, Zung Self-Rating Anxiety Scale;

SSRS, Social Support Rating Scale.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all enrolled parturients. The study was conducted in accordance with the Declaration of Helsinki and Chinese clinical trial research regulations. The study protocol was approved by the Shenzhen Maternity and Child Healthcare Hospital Ethics Committee (Approval No. SZFY2017102095). and the study was registered in the China Clinical Registration Center (Registration No. ChiCTR-OOC-17013164). Written informed consent was obtained from all participants.

Consent for publication

All participants have given consent for publication.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interest

We declare that we have no conflict of interest.

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Authors' contributions

GHL, XFQ contributed to the design of the study, data analysis and interpretation, manuscript drafting and review. XHT, MGW, HW, XGW, JS, and YL contributed to the design of the study, data analysis, data interpretation and review of manuscript to be published. YTL, XLH and PWcontributed to the conception and design of the study, and review of manuscript to be published.

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Figures

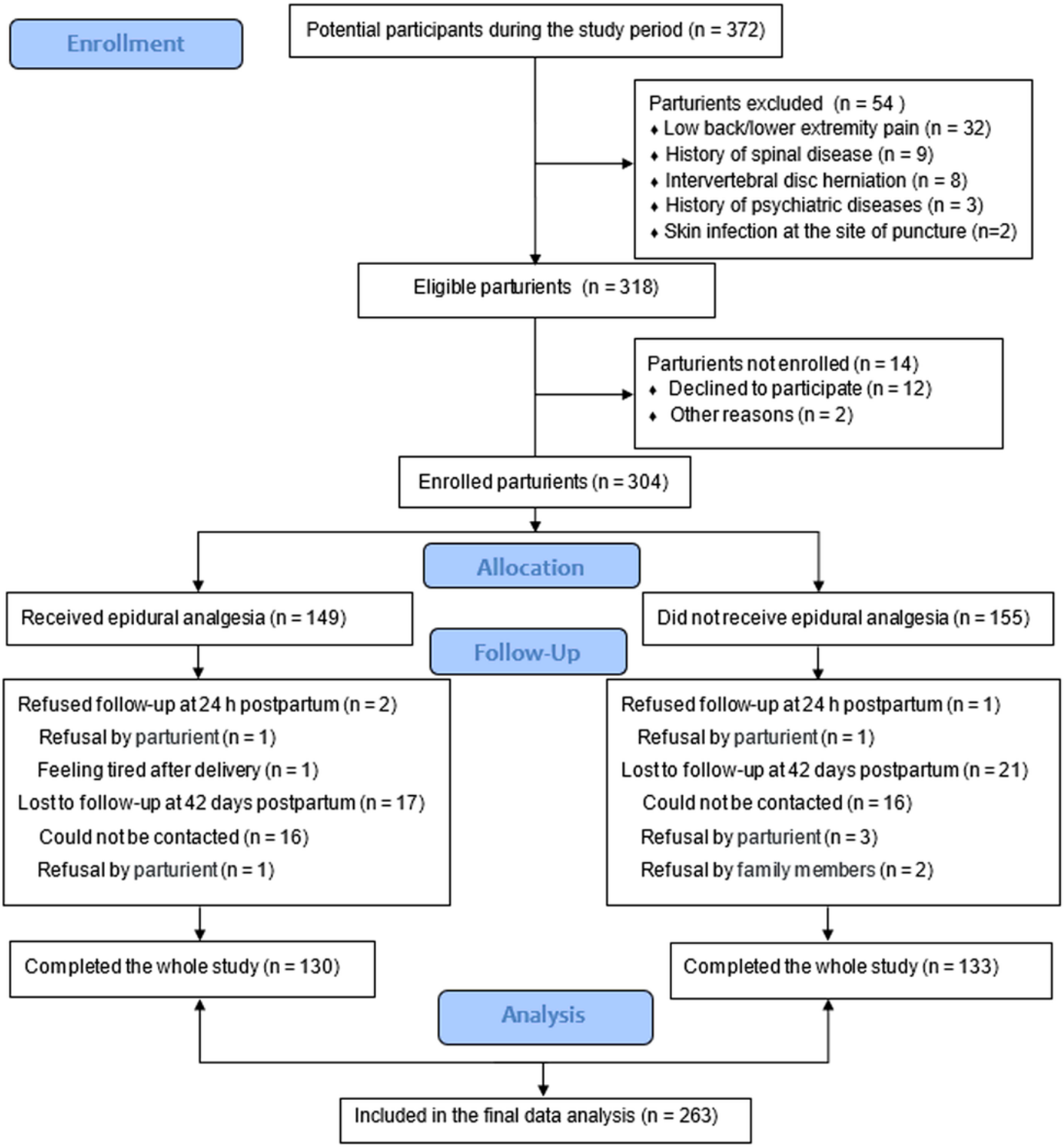

Figure 1

Flow chart of patient enrollment.

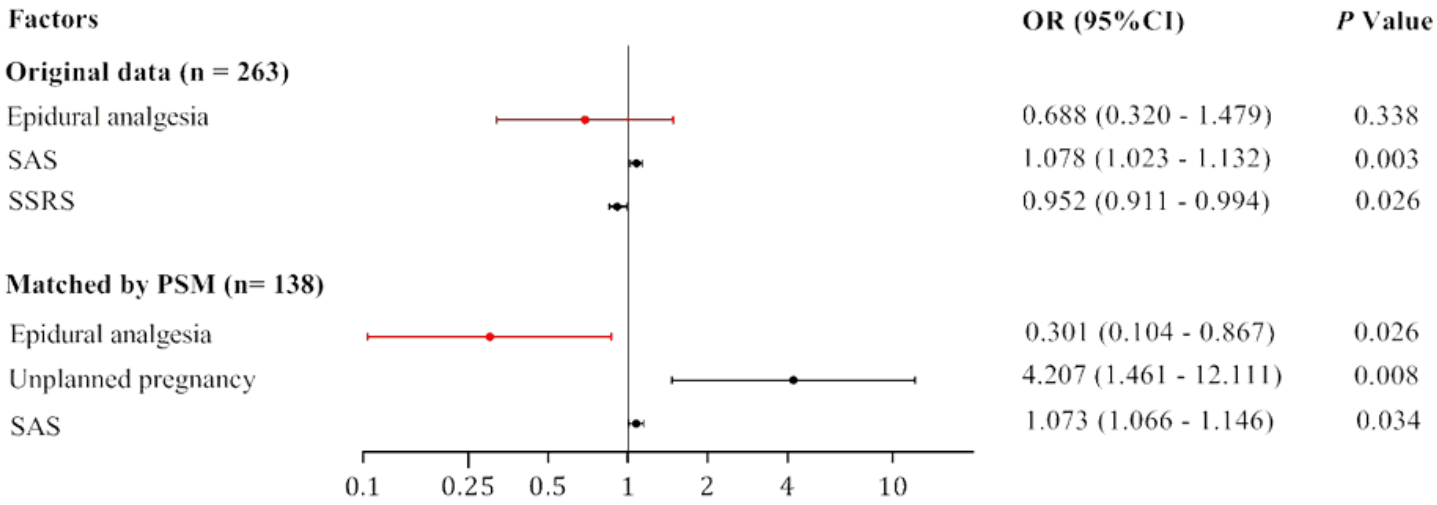

Figure 2

Independent influencing factor□IIF□on PPD at 24 h post-delivery before and after propensity matching (PSM).

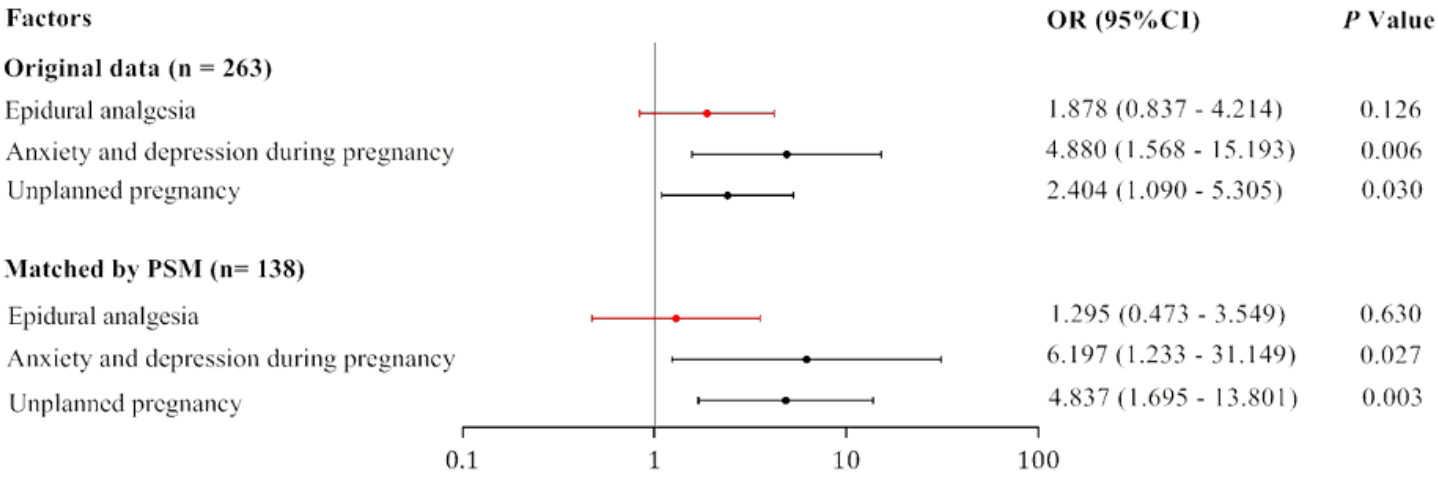

Figure 3

IIF on PPD at 42 days before and after PSM

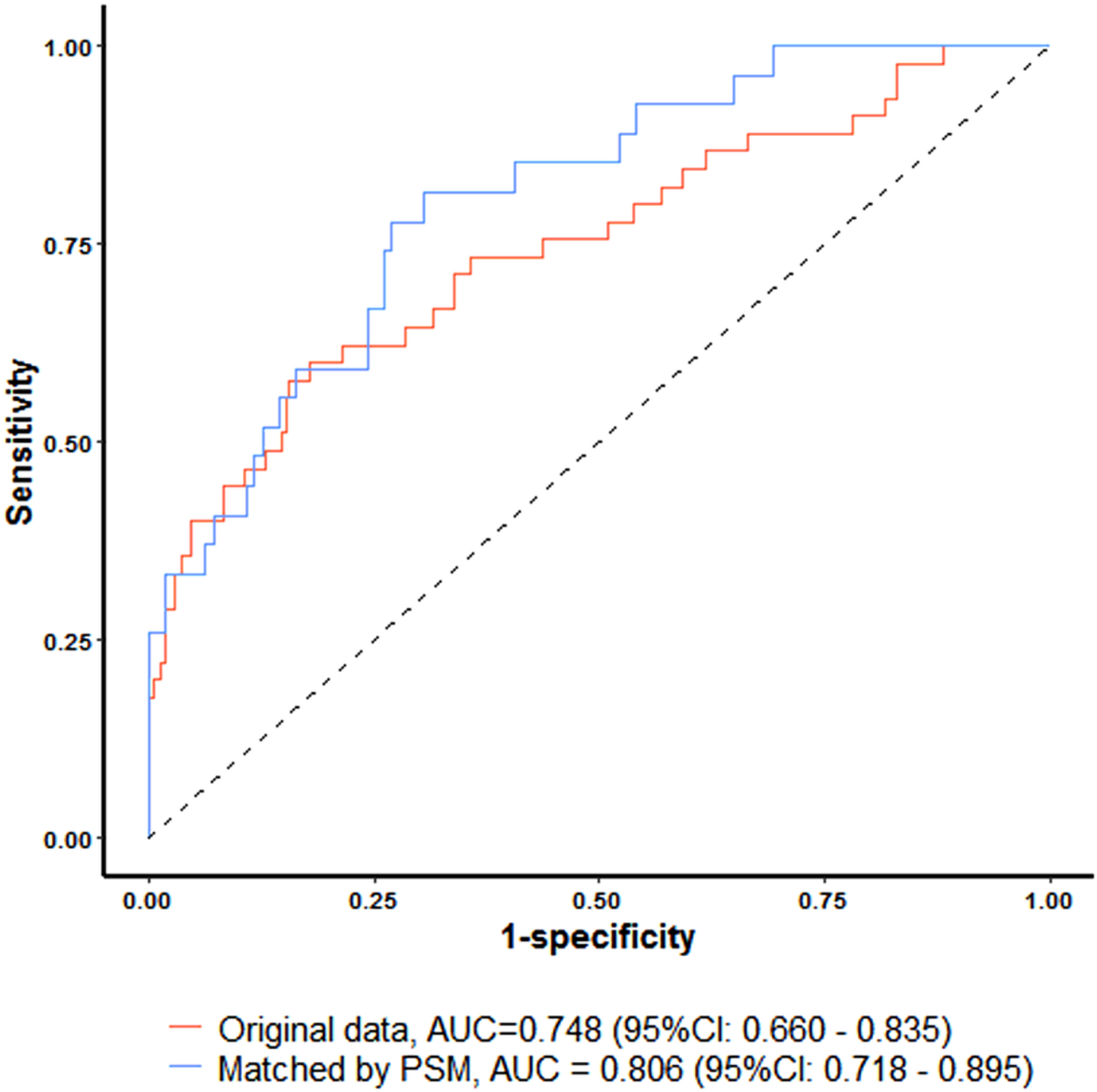

Figure 4

ROC curves on PPD at 24 h post-delivery before and after PSM

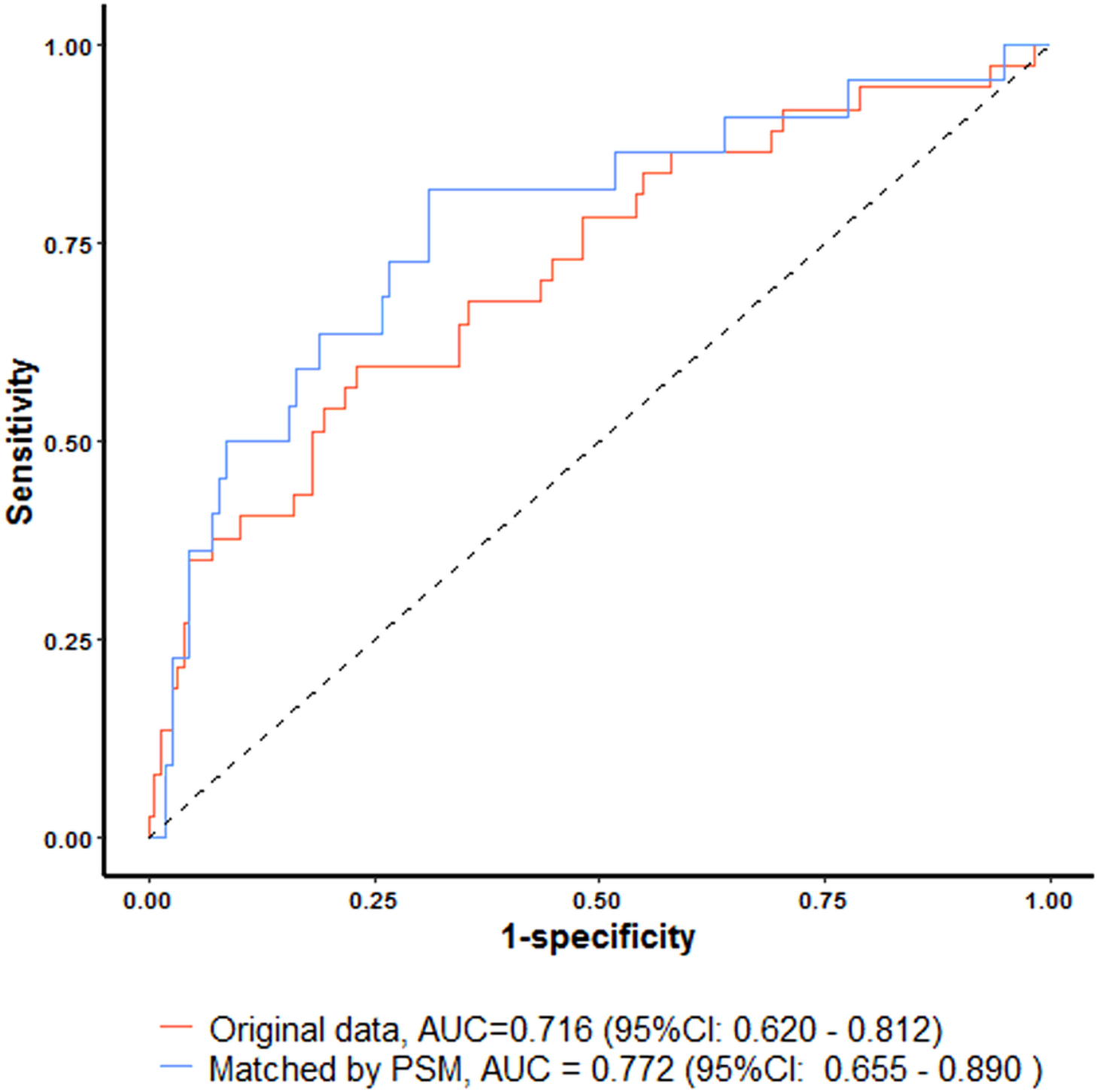

Figure 5

ROC curves on PPD at 42 days before and after PSM

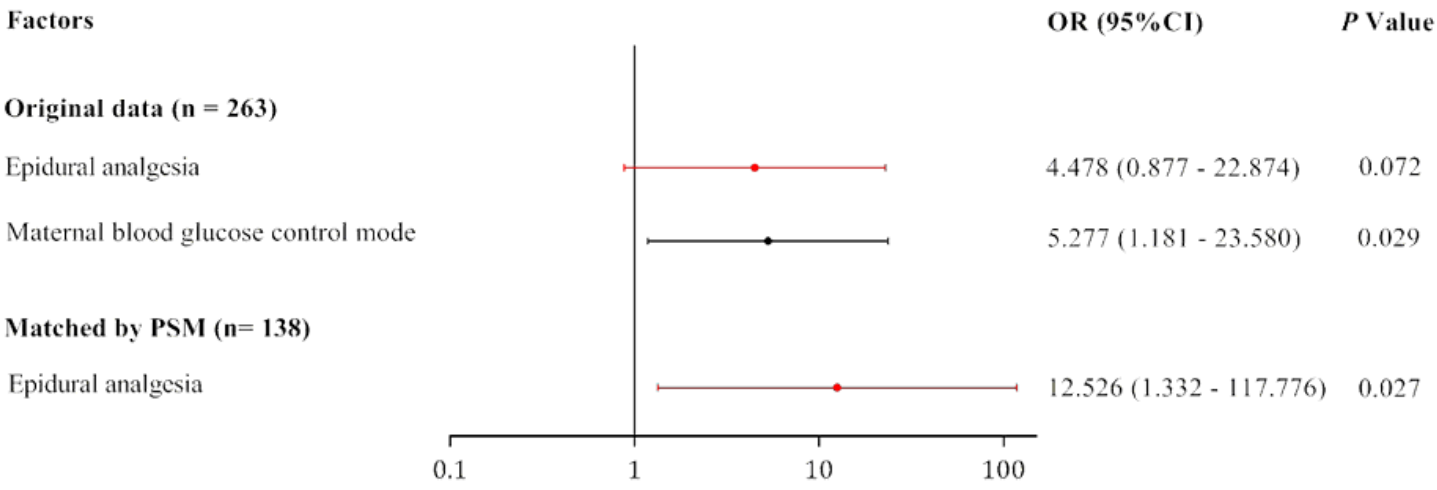

Figure 6

IIF on the rate of neonate transfer to the NICU for hypoglycemia treatment before and after PSM

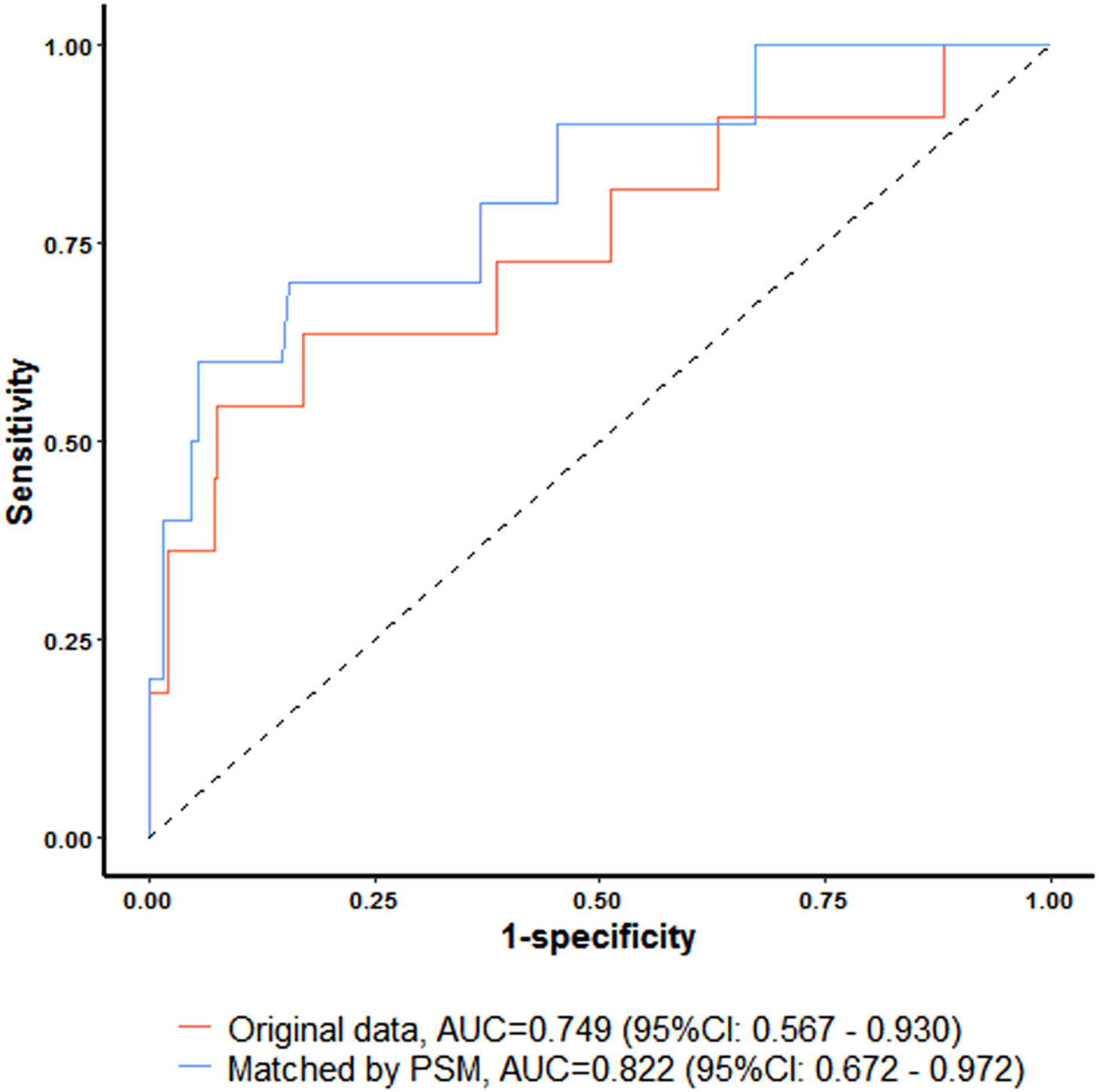

Figure 7

ROC curves on the rate of neonate transfer to the NICU for hypoglycemia treatment before and after PSM