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Original Article

Perinatal outcome and influencing factors of intrauterine transport in high-risk pregnancy with gestational ≤ 34 weeks

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Abstract: To analyze the perinatal outcome and influencing factors of intrauterine transport in high-risk pregnancies with gestational age ≤ 34 weeks. A total of 118 high-risk pregnancies with gestational age ≤ 34 weeks treated in our hospital from January 2017 to April 2020 were selected as the intrauterine transport group. According to perinatal outcome, the intrauterine transport pregancy were divided into a favorable group and a poor group. At the same time, 100 cases of preterm delivery (neonatal transport) were selected as the control group. Univariate analysis and multivariate Logistic analysis were performed to analyze the clinical data of the participants. The 118 high-risk pregnancies with gestational age ≤ 34 weeks were transported to Children's Hospital of Hebei province; 41 cases were given symptomatic support after hospitalization and pregnancy period extended; 22 cases had postpartum hemorrhage (transfusion therapy was required); 105 cases were live births and 13 cases were perinatal deaths. The incidence of complications in the intrauterine transport group was significantly lower than that in the control group ($P < 0.05$). Univariate analysis showed that there were differences in AFP, β-hCG, whether the uterine orifice opened before transport, vital signs before transfer, and whether there was contraction before transport between the two groups ($P < 0.05$). Logistic regression analysis showed that AFP ≥ 1.98 ng/mL, β-hCG ≥ 2.05 IU/L, opened uterine orifice before transport, unstable vital signs before transport, and contractions before transport were influencing factors for intrauterine transport of perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks ($P < 0.05$). Intrauterine transport is superior to neonatal transport. Therefore, early intrauterine transport should be considered to avoid delay in treatment, and transportation should be implemented on the basis of a comprehensive evaluation of the transfer plan to improve the perinatal outcome.

Keywords: High-risk pregnancy, intrauterine transport, perinatal outcome, influencing factors

Introduction

Perinatal transport in the clinic primarily includes neonatal transport and intrauterine transport. Neonatal transport is likely to cause cold injury, hypoxia, poor circulation, acidosis, and bumps during transport, which can result in serious complications such as neonatal pulmonary hemorrhage and intracranial hemorrhage [1-3]. Therefore, intrauterine transport is highly clinically recommended, since the mother is the optimal incubator for newborn transport. Intrauterine transport refers to transferring the pregnant women to medical units with favorable medical conditions and being able to provide neonatal intensive care unit (NICU) and organ support treatment before delivery [4], thus ensuring the pregnant women's and fetuses' access to sophisticated medical resources and further improving the perinatal outcome. It is clinically found that there is a chance of poor perinatal outcomes with intrauterine transport in high-risk pregnancies with gestational age ≤ 34 weeks. The exploration of influencing factors for the perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks can be conducive to determine which type of pregnant women is best suitable for intrauterine transport; in which the suitable ones benefit, and the unsuitable ones opt for other optimal treatment in a timely manner. This study selected intrauterine transport of hi-

gh-risk pregnancies with gestational age ≤ 34 weeks as the research subjects; explored the perinatal outcome of intrauterine transport, and analyzed the outcomes using univariate analysis and multivariate analysis, aiming to explore the influencing factors of the perinatal outcome of intrauterine transport in high-risk pregnancies with gestational age ≤ 34 weeks and provide a reference for intrauterine transport.

Materials and methods

General information

This study was a retrospective analysis. A total of 118 pregnant women with high-risk pregnancies with gestational age ≤ 34 weeks who were admitted to Children's Hospital of Hebei Province from January 2017 to April 2020 were selected as the intrauterine transport group. A total of 100 cases of premature neonates aged 0 to 3 days transported during the same period were selected as the control group. Inclusion criteria: ① women having complete clinical data; ② women with singleton pregnancy and gestational age ≤ 34 weeks; ③ women displaying transport indications. Intrauterine transport: severe gestational hypertension or other hypertension-induced complications, fetal malformations, intrauterine growth retardation, poor birth progress, fetal malposition, etc. Neonatal transport: weak body, body weight < 2.5 kg, or extremely immature physiological and metabolic functions; ④ women and their families knowing about the study and having signed a consent form before transport. Exclusion criteria: ① women with unnatural conception, such as assisted reproductive technology conception; ② women having a history of mental illness or cognitive impairment. This study was approved by the ethics committee of Children's hospital of Hebei province.

Methods

Data collection: Intrauterine transport data includes maternal age, gravidity, parity, gestational weeks of transport, platelet (PLT), alpha-fetoprotein (AFP), β human chorionic gonadotropin (β-hCG), uncojugated estriol (UE3), whether the uterine orifice has been opened before transport, the vital signs before transport, whether there is contraction before transport, delivery modes, etc. The neonatal transport data includes maternal age, gravidity, parity, gestation week, the newborn weight, and neonatal complications, etc. The detection methods of maternal PLT, AFP, β-hCG, UE3 are: collect 5 mL fasting venous blood of the pregnant women in the early morning, Sysmex XN-9000 automatic blood cell analyzer was used to detect PLT level, and AC-CESS automatic chemistry luminescence immunoassay analyzer was used to detect the levels of AFP, β-hCG and UE3.

Subgroups of intrauterine transport: According to the perinatal outcomes of the intrauterine transport group, they were divided into subgroups including poor outcome group (fetal death, neonatal pneumonia, neonatal intracranial hemorrhage, neonatal sepsis, neonatal asphyxia, etc.) and favourable outcome group (those without the above situations).

Statistical analysis

Statistical analysis was performed using SPSS 19.0 statistical software. The enumerated data was expressed as a ratio (%) and analyzed by the chi-square test. The chi-square test was usually used in the statistical inference of categorical data, including the chi-square test for comparing two rates or two constituent ratios, multiple rates or chi-square test of multiple composition ratio comparison. The measured data is expressed as (mean ± standard deviation) and analyzed by t-test. The t-test uses t-distribution theory to infer the probability of the difference, so as to compare whether the two averages are significantly different. Single factor and multivariate logistic regression analysis were used to investigate the related factors of intrauterine transportation of high-risk pregnancies with gestational age ≤ 34 weeks. Univariate analysis refers to the analysis of a certain variable at a point in time. Multi-factor analysis refers to a series of statistical analysis methods for the relationship between multiple factors and the relationship between these factors. Multi-factor analysis is mainly used to explain the direction and extent of the influence of each factor on the total change when the total change of a phenomenon is affected by three or more. ROC curve analysis was also performed on AFP and β-hCG indicators to predict the perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks. The ROC curve is a series of different binary classifica-

Table 1. Comparison of general data and complications between intrauterine transport group and control group

Factors	Intrauterine transport group (n = 105)$^{\Delta}$	Control group (n = 100)	t/χ^2	*P*
Maternal age (year)	29.53±3.76	29.68±3.85	0.282	0.778
Gravidity (times)	2.39±0.65	2.41±0.62	0.225	0.822
Parity (times)	1.09±0.32	1.12±0.33	0.661	0.509
Delivery gestational age (week)	31.25±3.67	30.46±2.95	1.694	0.092
Newborn birth weight (kg)	2.72±0.68	2.56±0.78	1.568	0.119
Neonatal complications of live birth			4.075	0.044
Pneumonia	4 (3.39)	7 (7.00)		
Intracranial hemorrhage	2 (1.69)	4 (4.00)		
Sepsis	7 (5.93)	10 (10.00)		
Asphyxia	5 (4.24)	8 (8.00)		

Note: $^{\Delta}$indicates that only live births were involved.

tion methods, with the true positive rate (sensitivity) as the ordinate and the false positive rate (1-specificity) as the abscissa. It is a comprehensive indicator reflecting the continuous variables of sensitivity and specificity. $P < 0.05$ was considered statistically significant.

Results

Perinatal outcomes of intrauterine transport of high-risk pregnancies with gestational age ≤ 34 weeks

A total of 77 of the 118 pregnant women delivered their babies within 24 hours, and 41 cases were given symptomatic support after hospitalization and pregnancy period was extended, and the gestational period ranged from 3 to 11 days. Delivery modes: there were 53 cases of vaginal delivery and 65 cases of cesarean section. Pregnant women outcome: there were 22 cases of postpartum hemorrhage (transfusion therapy was required), 96 cases with no postpartum hemorrhage (transfusion therapy was not required), and no maternal death occurred. Neonatal outcomes: there were 105 live births and 13 perinatal deaths. Neonatal complications: 4 cases of pneumonia, 2 cases of intracranial hemorrhage, 7 cases of sepsis, and 5 cases of asphyxia.

Comparison of general data and complications between intrauterine transport group and control group

There was no significant difference in the maternal age, gravidity, parity, gestational age, and birth weight between the intrauterine transport group and the control group ($P > 0.05$). The incidence of complications of live births in the intrauterine transport group was significantly lower than that in the control group, and the difference was statistically significant ($P < 0.05$, **Table 1**).

Univariate analysis of perinatal outcomes of high-risk pregnancies with gestational age ≤ 34 weeks

Among 118 cases of perinatal outcomes of high-risk pregnancies with gestational age ≤ 34 weeks, 31 cases had poor perinatal outcomes, accounting for 26.27% (31/118), and 87 cases had favourable perinatal outcomes, accounting for 73.73% (87/118). Univariate analysis showed that there was no statistically significant difference between the poor group and the favourable group in the age, gravidity, parity, gestational week, PLT, UE3, and delivery modes ($P > 0.05$). There were differences in AFP, β-hCG, whether the uterine orifice opened before transport, vital signs before transfer, and whether there was contraction before transport between the two groups ($P < 0.05$, **Table 2**).

ROC curve analysis of serum AFP and β-hCG indicators to predict the perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks

Serum AFP expression level was superior to β-hCG content in predicting the outcome of intrauterine transport of high-risk pregnancies

Table 2. Univariate analysis of perinatal outcomes of high-risk pregnancies with gestational age ≤ 34 weeks

Factors	Poor outcome group (n = 31)	Favorable outcome group (n = 87)	t/χ^2	*P*
Maternal age (year)	29.75±3.84	29.62±3.93	0.159	0.874
Gravidity (times)	2.36±0.63	2.43±0.65	0.519	0.605
Parity (times)	1.13±0.32	1.17±0.34	0.571	0.569
Delivery gestational age (week)	31.49±3.47	30.92±3.16	0.840	0.402
PLT (10^9/L)	118.93±17.53	117.64±19.24	0.328	0.743
AFP (ng/mL)	2.46±0.58	1.43±0.39	11.020	< 0.001
β-hCG (IU/L)	2.34±0.67	1.29±0.38	10.630	< 0.001
UE3 (nmol/L)	0.78±0.19	0.84±0.23	1.302	0.195
Whether uterine orifice opened before transport			8.066	0.005
Yes	5 (71.43)	2 (28.57)		
No	26 (23.42)	85 (76.58)		
Vital signs before transport			7.782	0.005
Stable	27 (23.89)	86 (76.11)		
Unstable	4 (80.00)	1 (20.00)		
Whether contractions occurred before transport			8.208	0.004
Yes	6 (66.67)	3 (33.33)		
No	25 (22.94)	84 (77.06)		
Delivery mode			0.654	0.419
Vaginal delivery	12 (22.64)	41 (77.36)		
Caesarean section	19 (29.23)	46 (70.77)		

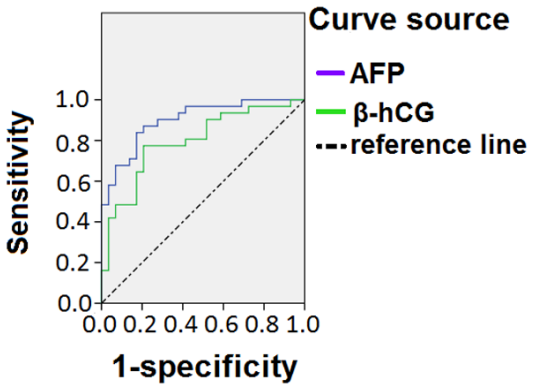

Figure 1. ROC curve analysis of serum AFP and β-hCG indicators to predict the perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks.

with gestational age ≤ 34 weeks, as shown in **Figure 1** and **Table 3**.

Multivariate logistic regression analysis of perinatal outcomes of high-risk pregnancies with gestational age ≤ 34 weeks

The indicators (AFP, β-hCG, whether the uterine orifice has been opened during transport, vital signs during transport, and whether there was contraction during transport) had statistical significance when analyzed by univariate analysis (**Table 2**) were taken as independent variables, with the cutoff values (**Table 3**) combined, and the outcome of intrauterine transport (0 = no, 1 = yes) was taken as the dependent variable, the assignment was shown in **Table 4**. Logistic regression analysis showed that AFP ≥ 1.98 ng/mL, β-hCG ≥ 2.05 IU/L, opened uterine orifice before transport, unstable vital signs before transport, contractions before transport were influencing factors for intrauterine transport of perinatal outcome of high-risk pregnancies with gestational age ≤ 34 weeks ($P < 0.05$, **Table 5**).

Discussion

With the advance of prenatal diagnosis technology and the development and popularization of neonatal surgery, various birth defects requiring immediate surgical treatment after delivery are the primary targets of intrauterine transport [5]. This study found that the incidence of complications of live neonates in the

Table 3. ROC curve analysis of serum AFP and β-hCG indicators

Parameters	Area under the curve (AUC)	Cutoff value	Sensitivity (%)	Specificity (%)	*P*	95% CI	
						Lower limit	Upper limit
AFP	0.903	1.98 ng/mL	84.70	91.40	0.005	0.728	0.989
β-hCG	0.807	2.05 IU/L	78.90	85.60	0.034	0.618	0.847

Table 4. The definition of relevant variables and assignment

Factors	Code	Assignment
AFP	X1	0 ≥ 1.98 ng/mL, 11.98 ng/mL
β-hCG	X2	0 ≥ 2.05 IU/L, 12.05 IU/L
Whether uterine orifice opened before transport	X3	0 = no, 1 = yes
Vital signs before transport	X4	0 = stable, 1 = unstable
Whether contractions occurred before transport	X5	0 = no, 1 = yes

Table 5. Multivariate logistic regression analysis of perinatal outcomes of high-risk pregnancies with gestational age ≤ 34 weeks

Variables	*β*	*SE*	*Wald* χ^2	*P*	*OR* (*95% CI*)
AFP ≥ 1.98 ng/mL	1.365	0.563	5.878	0.016	3.915 (2.095~13.158)
β-hCG ≥ 2.05 IU/L	1.179	0.485	5.909	0.013	3.251 (1.392~11.846)
Whether uterine orifice opened before transport	0.894	0.308	8.425	0.005	2.445 (1.308~8.274)
Vital signs before transport	1.799	0.617	8.501	0.004	6.043 (3.627~21.168)
Whether contractions occurred before transport	0.948	0.347	7.464	0.008	2.581 (1.785~13.535)

intrauterine transport group was significantly lower than that in neonatal transport, indicating that patients are properly treated after intrauterine transport with high-risk pregnancies to the NICU with advanced medical conditions, due to sophisticated medical and equipment level. However, intrauterine transport is not available for all pregnant women. In this study, the perinatal outcomes of 118 cases of intrauterine transport with high-risk pregnancies with gestational age ≤ 34 weeks were statistically analyzed. It was found that 22 cases had postpartum hemorrhage, 13 cases had perinatal deaths, 4 cases had neonatal pneumonia, 2 cases had neonatal intracranial hemorrhage, 7 cases had neonatal sepsis and 5 cases of neonatal asphyxia occurred, demonstrating that the proportion of poor perinatal outcomes in intrauterine transport is still high. This may be related to the inadequate risk assessment before transport. Therefore, it is imperative to comprehensively evaluate the risks and benefits of transport. If the disadvantages outweigh the advantages, then intrauterine transport should be suspended.

This study revealed that serum AFP ≥ 1.98 ng/mL, β-hCG ≥ 2.05 IU/L, opened uterine orifice before transport, unstable vital signs before transport, and contractions before transport were influencing factors for the outcomes of intrauterine transport in high-risk pregnancies with gestational age ≤ 34 weeks. This is similar to the results of Jacqueline Lagendijk et al. [6]. The following may be attributed to these results: AFP is the most common globulin in fetal serum, and is secreted by the yolk sac in early pregnancy and by the fetal liver in late pregnancy. It penetrates the placental villi tissue and enters the maternal circulation, shows an increasing trend in early and mid-pregnancy, and reaches relative stability at 32 weeks. When chorionic function is abnormal or diseased, its permeability increases and maternal serum AFP levels tend to increase significantly [7]. Studies have shown that the increase in AFP MoM value is related to the increased risk of poor pregnancy outcomes such as preeclampsia, fetal growth restriction, premature rupture of membranes, stillbirth, miscarriage, etc. [8-12]. Therefore, when the AFP level of pregnant women is abnormally elevated, it is urgent to consider early intrauterine transport to an advanced medical unit. β-hCG is a glycoprotein secreted by placental syncytiotrophoblast cells [13], which increases rap-

idly from the beginning of pregnancy to the 8th week, then decreases, and relatively stabilizes at 18-20 weeks [14-17]. It is reported that β-hCG MoM value ≥ 2.2 is related to the risk of hypertension during pregnancy, miscarriage, low infant weight, and intrauterine death [18, 19]. Under pathological conditions, placental trophoblasts proliferate in hypoxic conditions, leading to increased secretion of β-hCG [20]. This study also found that the level of β-hCG in the poor perinatal outcome group was higher than that in the good outcome group, which was basically consistent with the above conclusion. It is suggested that the application of intrauterine transport for mother's whose uterine orifice has been opened before transport and who will likely give birth in a short period of time may affect the perinatal outcome due to the bumps and transport time. Therefore, whether the transport route is smooth and the amount of time required for transport should be fully evaluated, or postpartum referral should be considered [21]. For pregnant women with unstable vital signs and contractions before transport, intrauterine transport will delay the treatment time and affect the perinatal outcome. For such pregnant women, we should first call a doctor in a superior hospital for a consultation and assistance until maternal vital signs stabilize. For high-risk pregnancies with gestational age ≤ 34 weeks, the nifedipine should be given as an intervention to inhibit contractions and preterm labor. Magnesium sulfate should be applied to protect the fetal nervous system and ensure the completion of glucocorticoids to promote fetal lung maturating. Transport to superior hospitals where mother's can be provided with higher treatment ability can be carried out when sufficient time is left through evaluation.

In summary, intrauterine transport is superior to neonatal transport for pregnant women with AFP ≥ 1.98 ng/mL, β-hCG ≥ 2.05 IU/L and gestational age ≤ 34 week. For pregnant women whose uterine orifice opens before transport, vital signs are unstable before transport, and contractions occur before transport, the transport should be implemented based on the full evaluation of transfer program and aiming to improve the perinatal outcome. Due to the retrospective quality, and insufficient sample size, the results may be biased. Thus, prospective studies or larger sample sizes are still needed for further study.

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Disclosure of conflict of interest

None.

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