

Analysis of Complications in Preterm Infants with Twin and Singleton of Different Gestational Ages

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Abstract: This study aimed to compare the complications of preterm twins versus singletons and analyze differences across gestational ages. Preterm twins delivered between 2 March 2022 and 6 November 2022 were compared to an age-matched control group of singletons, involving 65 twins and 103 singletons. The most common complication in premature infants was neonatal jaundice (87.72%), followed by patent foramen ovale (79.76%) and neonatal respiratory distress syndrome (NRDS) (57.14%). Twins had significantly higher Apgar scores at 1, 5, and 10 minutes compared to singletons. However, twins showed a higher incidence of ventricular septal defect (VSD) (7.69%) than singletons, with a statistically significant difference. In contrast, twins exhibited significantly lower rates of neonatal jaundice (78.46%), electrolyte imbalance (18.4%), and acid-base imbalance (9.23%) compared to singletons. Furthermore, as gestational age increased, the incidence of intrauterine infection, electrolyte and acid-base imbalances, neonatal coagulation disorders, patent ductus arteriosus (PDA), anemia, and NRDS in preterm infants gradually decreased, with all differences reaching statistical significance ($P < 0.05$). These findings highlight the importance of close monitoring and timely management of complications in premature infants to prevent severe outcomes.

Keywords: Neonatal; Diseases; Premature; Twin; Singleton; Gestational age

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1. Introduction

Two to four percent of all births are twins. Twins face higher risks throughout the entire pregnancy process, but less than 50% can persist until full term. Premature birth refers to the birth before 37 gestation weeks. According to the gestational age, premature infants can be further divided into extremely premature infants (gestational age less than 28 weeks), very premature infants (gestational age 28–31 + 6 weeks), moderate premature infants (gestational age 32–33 + 6 weeks), and late premature infants (gestational age 34–36 + 6 weeks). This classification is based on the growth and development of infants and plays a crucial role in determining their clinical characteristics

and prognosis during the perinatal period. Premature birth mainly involves respiratory, circulatory, digestive, neurological, and thermoregulatory issues.

The factors that affect the prognosis of premature infants include maternal factors, fetal factors, and perinatal management. There are differences in birth conditions, causes, appearance, and physiological characteristics between singleton and twin premature infants. To better understand the influence of maternal and fetal factors on premature infants, this study analyzed and compared the perinatal data of 168 premature infants of varying gestational ages admitted to the neonatal intensive care unit of Dongguan Maternal and Child Health Care Hospital. It examined whether there were differences between singleton and twin premature infants and explored whether being a singleton or twin increased the risk of adverse perinatal outcomes.

2. Materials and methods

2.1. Design

This study used questionnaires to conduct a cross-sectional and descriptive analysis. Once the babies were released from the hospital, the diagnoses were obtained.

2.2. Subjects

The premature infants were admitted to Dongguan Maternal and Child Health Care Hospital. They were chosen using purposive sampling. The inclusion criteria were less than 37 gestation weeks, with the mother's informed consent and voluntary involvement in the study. The infants were excluded with the following criteria: death, transfer to another hospital, and discharge against doctor's orders.

Because of the small sample size, the sample group was divided into three groups based on gestational age. There were 32 cases (22 singleton and 10 twins) in the extremely premature infant group (gestational age 28–31 + 6 weeks), 39 cases (23 singleton and 16 twins) in the moderate premature infant group (gestational age 32–33 + 6 weeks), and 97 cases (58 singleton and 39 twins) in the late preterm infant group (gestational age 34–36 + 6 weeks).

2.3. Research instrument

Maternal age and pregnancy complications were recorded, including gestational diabetes mellitus (GDM), anemia, gestational hypertension, hypothyroidism during pregnancy, and placenta previa. Conditions for preterm infants included mode of conception, birth weight, gender, and complications. More than twenty complications were identified in the study, including anemia, intrauterine infection, acid-base imbalance, neonatal pneumonia, neonatal coagulation disorders, neonatal jaundice, patent foramen ovale, neonatal hypoglycemia, patent ductus arteriosus (PDA), neonatal respiratory distress syndrome (NRDS), electrolyte imbalance, ventricular septal defect (VSD), retinopathy of prematurity, choroid plexus cyst, subependymal cysts, functional gastrointestinal disorders, neonatal sepsis, hydrocele testis, pulmonary hypertension, elevated bile acids, bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH).

2.4. Data collection and analysis

Data were collected from March 2022 to November 2022. All statistical analyses were performed using SPSS version 26.0. Measurement data were expressed as mean \pm standard deviation, while count data were presented as frequency and component ratio. Comparisons between groups were conducted using χ^2 tests and Fisher's exact

tests, with a P -value < 0.05 considered statistically significant.

2.5. Ethics statement

This study was approved by the Medical Ethics Committee of Dongguan Maternal and Child Health Care Hospital (2022-1).

3. Results

3.1. Demographic data

The premature babies included 106 boys and 62 girls, and the male/female ratio was 1.710. There was no significant difference between singleton and twins in sex composition ratio ($P = 0.746$). The mean birth weight was 2024.8 g (SD = 497.42, range = 900–3230 g), ($P = 0.801$). One hundred and eleven (66%) premature infants' birth weight was mainly between 1500 and 2500 g.

There was no significant difference between singletons and twins at different gestational weeks. The baseline information remained consistent and comparable across the study ($P = 0.628$). The average length of these premature babies' hospital day was 19.56 days (SD = 17.35, range = 2–86 days).

3.2. Complications

3.2.1. Mother's pregnancy-related complications

Pregnant women who are expected to reach or exceed the age of 35 during childbirth are considered advanced-age mothers. There is no statistical age composition difference (advanced age and appropriate age group) between the mother of twin versus singleton ($P = 0.582$). Nineteen mothers reported a history of obstetrical complications, including miscarriage, premature delivery, dystocia, and stillbirth. However, there was no significant difference in obstetrical history when compared with 103 singleton pregnancies during the same period ($P = 0.523$).

Nearly two-thirds (91/139) of the mothers had pregnancy-related complications other than preterm birth. Aside from twin pregnancies and preterm birth, 33.3% (12/36) of mothers of twins experienced pregnancy complications, which was significantly lower than the 53.3% (55/103) observed among mothers of singletons ($P = 0.038$). Among the mothers of twins, 8 (22.22%) had gestational diabetes mellitus (GDM), 7 (19.44%) had anemia during pregnancy, 2 (5.56%) had gestational hypertension, and 1 (2.78%) had hypothyroidism during pregnancy. There was no significant difference compared with 103 single pregnancies, which could be seen in **Table 1**.

Table 1. Comparison of the mother's incidence of common complications

Complications	Singleton pregnancy (n = 103)	Twin pregnancy (n = 36)	χ^2	P
Anemia during pregnancy	16	7	0.295	0.587
GDM	22	8	0.012	0.914
Gestational hypertension	16	2	2.356	0.125
Hypothyroidism during pregnancy	5	1	0.279	0.598

3.2.2. Premie complications

Compared to singleton (3/103), twin preterm infants (16/65) were more likely conceived through in vitro fertilization ($P < 0.05$). Apgar scores of the twins are statistically higher than those of singleton, which were

available in **Table 2**.

Table 2. Comparison of the premature infants' Apgar scores

Characteristic	Single birth (n = 103)	Twin births(n = 65)	F	P
1 min Apgar score	9.62 ± 1.09	9.85 ± 0.48	F = 9.790	.002*
5 min Apgar score	9.87 ± 0.52	9.97 ± 0.17	F = 8.448	.004*
10 min Apgar score	9.92 ± 0.30	10	F = 19.208	.000*

3.2.3. Distribution of disease varies among single/twin preterm infants

Neonatal jaundice, patent foramen ovale, NRDS, and neonatal coagulation disorders rank among the top four complications in single/twin preterm infants. The fifth ranked complication in all the preterm infants is PDA. The fifth complication of twin pregnancy is neonatal hypoglycemia and neonatal coagulation disorders, while singleton pregnancy is PDA.

Multiple pregnancies were categorized as high-risk pregnancy. The incidence of low birth weight, neonatal coagulation disorders, IVH, choroidal plexus cysts, and hydrocele testis is higher in twin premature infants than in singleton infants. The incidence of neonatal jaundice, acid-base imbalance, and electrolyte imbalance in twin was significantly lower than that in single neonates, while the incidence of VSD in twin was significantly higher than that in single neonates. See **Table 3** for details and incidence rate of other diseases.

Table 3. Comparison of complication in premature infants n(%)

Complications	Single birth (n = 103)	Twin births (n = 65)	F	P
Neonatal jaundice	93(90.29%)	51(78.46%)	4.554	0.033*
Patent foramen ovale	83(80.58%)	51(78.46%)	0.111	0.739
Low birth weight	82(79.61%)	56(86.15%)	1.163	0.281
NRDS	61(59.22%)	35(53.85%)	0.471	0.493
Neonatal Coagulation disorders	40(38.83%)	23(35.38%)	0.202	0.653
PDA	39(37.86%)	21(32.31%)	0.536	0.464
Electrolyte Imbalance	35(33.9%)	12(18.40%)	4.763	0.029*
Anemia	33(32.04%)	15(23.08%)	1.568	0.210
Intrauterine infection	26(25.24%)	13(20%)	0.614	0.433
Neonatal hypoglycemia	23(22.33%)	23(35.38%)	3.416	0.065
Acid-base imbalance	23(22.33%)	6(9.23%)	4.788	0.029*
Neonatal pneumonia	19(18.45%)	10(15.38%)	0.262	0.609
Pulmonary hypertension	12(11.65%)	2(3.08%)	3.835	0.050
Intraventricular hemorrhage	10(9.71%)	8(12.31%)	0.281	0.596
Bronchopulmonary dysplasia	10(9.71%)	5(7.69%)	1.448	0.229
Subependymal cysts	9(8.74%)	1(1.54%)	3.690	0.055
Retinopathy of prematurity	7(6.8%)	4(6.15%)	0.027	0.870
Functional gastrointestinal disorders	6(5.83%)	2(3.08%)	0.664	0.415

Table 3 (Continued)

Complications	Single birth (n = 103)	Twin births (n = 65)	F	P
Elevated bile acids	6(5.83%)	1(1.54%)	1.834	0.176
Hydrocele testis	3(2.91%)	2(3.08%)	0.004	0.951
Neonatal sepsis	2(1.94%)	1(1.54%)	0.037	0.848
VSD	1(0.97%)	5(7.69%)	5.228	0.022*
Choroid plexus cyst	1(0.97%)	4(6.15%)	3.707	0.054

3.2.4. Distribution of gestational age for the top ten diseases

The top 10 diseases of different gestational ages are different. The incidence of intrauterine infection, acid-base imbalance, electrolyte imbalance, PDA, neonatal coagulation disorders, NRDS, anemia, and newborn jaundice varies significantly among preterm infants of different gestational ages ($P < 0.05$).

Extremely preterm infants had a statistically higher incidence of PDA, intrauterine infection and electrolyte imbalance than late preterm infants. With the increase of gestational age, the incidence of anemia and NRDS decreased statistically significantly. Extremely preterm infants exhibited a statistically significant higher incidence of neonatal coagulation disorders compared to moderate and late preterm infants. Extremely preterm infants also had a statistically higher incidence of acid-base imbalance than moderate preterm infants as shown in **Table 4** below.

Table 4. Distribution of gestational age for the top ten diseases

Characteristic	Extremely preterm infants (n = 32)	Moderate preterm infants (n = 39)	Late preterm infants (n = 97)	χ^2	P
Patent foramen ovale	29 ^a	33 ^a	72 ^a	4.749	0.093
NRDS	31 ^a	29 ^b	36 ^c	41.238	0.000*
Neonatal coagulation disorders	22 ^a	12 ^b	29 ^b	16.480	0.000*
PDA	18 ^a	13 ^{a,b}	29 ^b	7.404	0.025*
Anemia	23 ^a	14 ^b	11 ^c	44.541	0.000*
Electrolyte imbalance	17 ^a	13 ^{a,b}	17 ^b	15.807	0.000*
Neonatal hypoglycemia	5 ^a	16 ^a	25 ^a	6.002	0.050
Intrauterine infection	16 ^a	11 ^{a,b}	12 ^b	19.823	0.000*
Acid-base imbalance	10 ^a	3 ^b	16 ^{a,b}	6.925	0.028*
Neonatal pneumonia	9 ^a	5 ^a	15 ^a	3.402	0.178

Due to the small sample size, conducting multiple rate comparisons for neonatal jaundice was impractical. Therefore, the sample was divided into two groups: extremely premature infants (28 to 33 + 6 weeks) and premature infants (34 to 36 + 6 weeks). The incidence of neonatal jaundice was significantly higher among

extremely premature infants (69/71) compared to premature infants (75/97), with a statistically significant difference ($\chi^2 = 13.209$, $P = 0.000$).

4. Discussion

4.1. Mother's pregnancy-related complications

Inconsistent with previous studies, there was no significant statistical difference in pregnancy complications (anemia, pregnancy induced hypertension) between twin and singleton, it may be related to the small sample size of the study ^[1].

4.1.1. GDM

This set of data shows that the prevalence of GDM is 21.5% (30/139), which is the most common complication. During the same period, the overall prevalence of gestational diabetes mellitus (GDM) in Mainland China was 14.8%, with higher rates reported in specific regions such as Chongqing at 26.2% and Xi'an at 27.44% ^[2-4]. Among the mothers of late preterm twin infants in this study, 13% (3/23) were diagnosed with GDM, which is consistent with the 13.2% reported in a study conducted in Shanghai ^[5]. GDM not only affects the mother's own health but also leads to adverse pregnancy outcomes. The high blood sugar levels in pregnant women with gestational diabetes mellitus (GDM) continuously stimulate the placenta and promote excessive insulin secretion by the fetus, which may lead to fetal hyperinsulinemia, antagonize adrenal cortical hormones, impair lung maturation, and increase the risk of neonatal respiratory distress syndrome (NRDS). Therefore, it is essential to pay close attention to prenatal check-ups, monitor blood glucose levels, and detect GDM as early as possible. Once diagnosed, pregnant women should actively cooperate with treatment, including correcting unhealthy lifestyle habits and using medications to maintain stable blood sugar levels, to reduce the risk of complications. Chinese studies have shown that multiple births are more likely to be associated with gestational diabetes combined with hypothyroidism ^[6]. However, in this study, no cases of gestational diabetes combined with hypothyroidism were observed.

4.1.2. Anemia

Anemia during pregnancy has a negative impact on the postnatal anemia, birth outcome, and growth and development of newborns ^[7]. Anemia significantly increases the incidence of complications such as gestational hypertension syndrome, postpartum hemorrhage, and preeclampsia in pregnant women. The ischemia and hypoxia of the uterus and placenta lead to fetal growth restriction, increasing the incidence of fetal distress, premature birth, stillbirth, and fetal death. The anemia gravidarum incidence of the study was 16.5% (23/139). Because this study is aimed at preterm infants, the incidence rate is slightly higher than 13.6% of the report on nutrition and chronic diseases of Chinese residents in 2020 ^[8].

Multiple pregnancies are a risk factor for anemia in pregnant women. Compared to singleton pregnancies, pregnant women with multiple pregnancies are more prone to anemia due to significant increases in blood volume and cardiac output. In this study, 26.09% (6/23) of mothers of late preterm twin infants had anemia, which is consistent with the 24.8% reported in a study from Shanghai ^[9].

It is essential to carry out pre-pregnancy and pregnancy health education for key populations to prevent the occurrence of anemia in pregnant women. Regular prenatal check-ups, especially monitoring hemoglobin (Hb)

and hematocrit (HCT) levels, are crucial for early detection and intervention. Strengthening the management of pregnant women with anemia through timely examinations, appropriate treatments, and dietary guidance can effectively improve maternal health. Additionally, when terminating pregnancy or during delivery, active measures should be taken to respond appropriately and minimize blood loss as much as possible.

4.2. Perinatal status of preemie

In this study, 55.3% of singleton mothers had complications, which was significantly higher than that of twin mothers. This suggests that premature singleton births may be more closely associated with the health status of pregnant women.

4.2.1. Apgar score

The Apgar score is mainly used to assess the degree of asphyxia at birth and the resuscitation effect. The lowering of oxygen carrying capacity in pregnant women results in the fetus experiencing low oxygen or hypoxia in the uterus, which affects Apgar. Only four neonates were considered to have mild asphyxia (Apgar score less than 7). Once physiological abnormalities are detected, neonatal resuscitation should be carried out immediately, followed by refined management to prevent multi-organ damage, disability, and death caused by hypoxia and ischemia, and improve the prognosis of newborns.

In this study, the Apgar scores of twin premature infants were significantly higher than those of singletons. Possible reasons include: (1) Twins are in a competitive state in the uterus, which may promote earlier adaptation to relatively unfavorable intrauterine environments compared to singletons; (2) Pregnant women expecting twins are generally more inclined to receive systematic prenatal care and regular examinations throughout pregnancy^[10]. Additionally, they are more likely to be admitted to hospitals with advanced medical technology and receive greater attention from obstetricians during delivery, contributing to better neonatal outcomes.

4.2.2. Neonatal jaundice

Premature delivery, low body weight, premature rupture of membranes, cesarean section, hypertensive disorder complicating pregnancy, diabetes complicating pregnancy, and fetal distress are independent risk factors for pathological jaundice in newborns^[11]. Premature infants are more likely to have neonatal jaundice. In this research group, the incidence rate of neonatal jaundice is 85.71% (144/168) lower than other research reports^[12, 13]. As gestational age increases, the incidence of jaundice shows a decreasing trend, consistent with previous research^[12, 14]. The incidence rate of jaundice in twin preterm infants was significantly lower than that in singleton. It may be related to early intervention for premature twin infants to avoid serious complications during the treatment process. The occurrence of jaundice is mainly related to immature liver development and a weak ability to process bilirubin in the blood. Distinguishing between physiological jaundice and pathological jaundice is crucial for developing a reasonable and effective treatment plan. If it is physiological jaundice, it can be temporarily observed without special treatment, but dynamic monitoring of transcutaneous bilirubin measurement is required. If it is pathological jaundice, it is recommended to actively undergo blue light irradiation treatment to promote the breakdown of bilirubin and prevent the occurrence of nuclear jaundice. But if it is severe jaundice, it is necessary to undergo blood exchange treatment as soon as possible. Additionally, it is crucial to investigate potential underlying causes such as infection, hemolysis, and other related conditions, initiate targeted treatment for the primary disease, and take timely measures to prevent complications.

4.2.3. NRDS

NRDS is the most common complication of the respiratory system in early preterm infants and the leading disease threatening their survival. More than half of the premature infants in this study suffered from NRDS. With the increase of gestational age, the incidence rate of NRDS shows a statistically significant downward trend, which is consistent with other research ^[12, 13]. In this study, the incidence rate of NRDS with gestational age < 34 weeks was 84.51% (60/71), higher than other studies, which were 52.16% ^[15]. Early identification, prevention, diagnosis, and treatment are key to NRDS management. Timely and effective resuscitation should be implemented after childbirth. For premature infants with spontaneous breathing, non-invasive ventilator CPAP mode assisted ventilation should be performed, and animal-derived pulmonary surfactant should be given as a substitute therapy as soon as possible. Mechanical ventilation should be avoided, or the duration of mechanical ventilation should be shortened as much as possible.

4.2.4. Neonatal coagulation disorders

The development of the coagulation system begins in the fetal stage and matures in adulthood. The levels of coagulation factors in newborns usually gradually increase with age ^[16]. Premature infants, due to immature liver development, have low levels and reduced activity of coagulation factors at birth, resulting in poor coagulation function. This deficiency may lead to an increased risk of bleeding, including intracranial hemorrhage and disseminated intravascular coagulation (DIC), which can pose life-threatening risks. According to this study, premature infants are more likely to suffer from neonatal coagulation disorders, and their incidence rate is 37.5% (63/168), higher than other research reports ^[12]. Extremely preterm infants (gestational age 28–31 + 6 weeks) had a statistically higher incidence of neonatal coagulation disorders than moderate and late preterm infants. The younger the gestational age, the more prone it is to coagulation dysfunction. Bo's research shows that both gestational hypertension and premature birth can affect the coagulation function of newborns ^[17]. Early identification and diagnosis are key to treating coagulation disorders ^[17]. Regularly conduct blood routine and coagulation function tests to promptly detect abnormalities in coagulation function. Once it occurs, medication should be taken as early as possible to treat the cause and symptoms.

4.2.5. Congenital heart disease

Small and medium-sized VSD are usually asymptomatic. Newborn with large VSD may exhibit feeding difficulties, weight loss, delayed growth and development, rapid breathing, and excessive sweating. VSD is the most common type of congenital heart disease, accounting for approximately 40% of all congenital heart abnormalities ^[18]. The incidence of VSD is approximately 1.35–17.3 cases per 1000 live births ^[19]. No report on incidence rate of premature infants. The incidence rate of VSD in preterm infants is 3.57% (6/168). Around 5/6 of VSD patients are twins. Pregnancy infection, premature birth, and non-first born babies are risk factors for congenital heart disease in twins. Small defects may self-heal during childhood. If the defect is large, has not healed for a long time, or is combined with other cardiac malformations, timely treatment can be carried out through surgical or internal medicine intervention, and the prognosis is good.

The ductus arteriosus is a pathway for blood circulation between the pulmonary artery and the aorta during fetal development ^[20]. The ductus arteriosus gradually closes after birth to form an arterial ligament. If it does not close, it is called PDA. PDA is a common congenital heart disease and a characteristic manifestation of

NRDS. Failure to close the ductus arteriosus can lead to pulmonary congestion and systemic ischemia, resulting in serious complications such as prolonged mechanical ventilation, bronchopulmonary dysplasia (BPD), BPD-related pulmonary hypertension, pulmonary hemorrhage, necrotizing enterocolitis (NEC), renal insufficiency, intraventricular hemorrhage (IVH), periventricular white matter softening, cerebral palsy, and even death^[21, 22].

According to the study, premature infants are more likely to have PDA, with an incidence rate of 35.71% (60/168), higher than other research reports^[12]. Extremely preterm neonates exhibited a significantly greater incidence of PDA than late preterm infants, consistent with previous research^[12]. A total of 12 out of 15 premature infants with a gestational age of < 30 weeks and 3 out of 4 premature infants with a gestational age of < 28 weeks developed PDA. Compared to other studies with 30% and 60%, the ratio of 75% is relatively high^[23]. It may be related to 6 twins among 16 premature infants under 30 weeks of gestation age. Conservative treatment, drug therapy, and surgical ligation can promote ductus arteriosus closure.

4.2.6. Electrolyte and acid-base disturbances

According to this study, premature infants are more likely to suffer from acid-base imbalance, and their incidence rate is 17.26% (29/168), consistent with previous research^[12]. The direct indicator of hypoxia and metabolic disorders is acid-base imbalance. Acid-base imbalance can greatly affect the metabolism of the body and the function of important organs. According to this study, premature infants are more likely to suffer from acid-base imbalances, such as hypoxemia caused by neonatal asphyxia, increased anaerobic fermentation, and lactate production, leading to metabolic acidosis. Neonatal lung infection and CO₂ retention lead to respiratory acidosis. Children receiving parenteral nutrition have an increased risk of metabolic acidosis due to premature and excessive use of amino acid products. Extremely preterm infants showed a much higher incidence of acid-base imbalance than moderate preterm infants.

Premature infants have fewer nephrons, immature glomeruli and tubules, low glomerular filtration rate, insufficient ability to regulate water and salt metabolism, low kidney response to aldosterone, reduced sodium reabsorption and excessive loss, and low clearance rates of potassium and chloride. Therefore, premature infants are prone to high levels of blood potassium, chloride, and hyponatremia. According to this study, the incidence rate of electrolyte imbalance is 27.98% (47/168), higher than Pang's research of 17.9%^[12]. Late preterm infants showed a much reduced incidence of electrolyte imbalance than extremely preterm infants. The imbalance of acid-base balance and electrolyte imbalance should be treated as early as possible for the primary disease and corrected with medication.

4.2.7. Anemia

Premature infants with immature liver and kidney development and a short lifespan of red blood cells may lead to anemia. The incidence rate of anemia in premature infants is 28.57% (48/168), conforming to the results of a previous study that showed results lower than 50.9% of other research reports^[7, 13]. With the growth of gestational age, anemia had a statistically significant incidence rate decline, consistent with previous research^[12]. The incidence of anemia in extremely premature infants was the highest (75%) and the lowest in late premature infants. The iron obtained by the fetus from the mother accounts for 60% of the total iron, so supplementing iron in late pregnancy is crucial for correcting and preventing iron deficiency anemia in the fetus. Delayed cord clamping or umbilical cord milking during delivery, supplementing iron after birth, using erythropoietin, infusing red blood cells, and reducing laboratory blood collection can be used to prevent and treat anemia of prematurity^[24].

During the application of antibiotics for treatment, bone marrow hematopoiesis is inhibited, leading to increased destruction of red blood cells. Therefore, preventing infections is also a crucial step in preventing anemia in premature infants.

4.2.8. Intrauterine infection

The infection of amniotic fluid, placenta (decidua, chorion, and amniotic membrane), and fetus caused by pathogenic microorganisms entering the amniotic cavity is called intrauterine infection ^[25]. Usually, intrauterine infection occurs in the fetus after infection during maternal pregnancy. In this study, the incidence rate of intrauterine infection with a gestational age of less than 34 weeks was 38% (27/71), lower than other research reports of 56.17% ^[15]. Late preterm infants showed a much reduced incidence of intrauterine infection than extremely and moderate preterm infants, consistent with previous research ^[26]. The late preterm infants had the lowest incidence of intrauterine infection (12.37%). Previous studies have shown that increased inflammatory mediators caused by intrauterine infections can inhibit the synthesis and secretion of pulmonary surfactant in premature infants. At the same time, these infants may respond poorly to external surfactant supplementation. This negatively affects lung development and maturation, increasing the risk of NRDS ^[15, 27]. If treatment is delayed, the mortality and teratogenicity rates are high. Intrauterine infection can cause damage or softening of fetal white matter, leading to the occurrence of fetal hypoxic-ischemic encephalopathy and brain damage, and in severe cases, death ^[28]. To ensure the life and health safety of newborns, prophylactic use of antibiotics is necessary for pregnant women at risk of intrauterine infection. The symptoms of intrauterine infection often lack specificity, mainly characterized by non-specific premature birth symptoms such as hypothermia, reduced crying, and feeding intolerance, making it difficult to diagnose clinically. Therefore, reliable inflammatory indicators are needed to assist in diagnosis and early standardized treatment.

5. Conclusion

In summary, the most common types of diseases in hospitalized premature infants during the neonatal period include neonatal jaundice, neonatal coagulation dysfunction, NRDS, Patent foramen ovale, etc. The disease spectrum varies among premature infants of different gestational ages. The outcome of twin premature infants was found to be better than that of singleton to some extent. Strengthening prenatal check-ups and health education during pregnancy is the key to avoiding premature birth. Early prevention, screening, diagnosis, and treatment of diseases of premature infants at different gestational ages are the key to reduce the incidence rate, mortality, and improve the cure rate. Due to the representativeness of the sample size, the results are somewhat limited, and further research in a large area is still needed to determine its long-term quality of life and prognosis.

Disclosure statement

The authors declare no conflict of interest.

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