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Comparative analysis of perinatal clinical problems in early and late preterm infants

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Summary

Objective: The aim of this study was to understand different clinical characteristics of early preterm infants (EPIs) and late preterm infants (LPIs). *Materials and Methods:* The clinical and laboratory data of 561 preterm infants, admitted to this hospital from January 2013 to December 2014, were comparatively analyzed. *Results:* EPIs accounted for 27.45% and LPIs accounted for 72.55%. The incidence rates of asphyxia at birth, placental abruption, and placenta previa in EPIs were significantly higher than those in LPIs ($p < 0.01$). The levels of albumin, globulin, triglycerides, serum phosphorus, serum iron, and hemoglobin in EPIs were significantly lower than those in LPIs ($p < 0.01$). The proportion of low body temperature, low blood sugar, respiratory distress, apnea and feeding intolerance, as well as assisted ventilation therapy, in EPIs were significantly higher than those in LPIs ($p < 0.01$). *Conclusions:* LPIs accounted for the majority of preterm infants, placental abruption and placenta previa were the unique risk factors in EPIs, EPIs had lower nutritional reserves than LPIs, and would be more susceptible to the perinatal complications.

Key words: Early preterm infants; Late preterm infants; Perinatal period.

Introduction

Late preterm infants (LPIs) refer to infants with gestational age as 34~36^{+6} weeks (with gestational age as 239~259 days after menstrua) [1-4], while early preterm infants (EPIs) refer to infants with gestational age as 28~33^{+6} weeks (with gestational age as 197~238 days after menstrua). EPIs accounted for about 10%-13% of all hospitalized PIs [5-7], and LPIs accounted for majority of PIs. In recent years, with the development of assisted reproductive technology, and the increasing advanced maternal age, the proportion of EPIs exhibited a rising trend, while the exact demographic data of PIs are not known. Currently, the comparison between early term infants (with gestational age as 37~38^{+6} weeks) and LPIs (with gestational age as 39~41^{+6} weeks) has been more carefully assessed [8-10], while the comparison between EPIs and LPIs is rare. This study statistically analyzed the clinical data of EPIs and LPIs, such as perinatal factors, biochemical indicators, and various complications at birth, etc., aiming to explore the strategies to further reduce mortality rate and improve clinical outcomes.

Materials and Methods

Study subjects

The study included 561 PIs, born and admitted into neonatal unit of the present hospital from January 2013 to December 2014, which were selected, including 154 EPIs and 407 LPIs. The infants that were discharged while re-hospitalized for other diseases were not included in this study. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Maternal and Child Health Hospital of Yiwu. Written informed consent was obtained from all participants' guardians.

Methods

The clinical data of PIs admitted into the present department: were retrospectively collected, including gender, gestational age, birth weight, delivery mode, maternal pregnancy complications (including hypertension, anemia, diabetes, cholestasis), obstetric factors (including birth asphyxia, premature rupture of membrane, placental abruption, placenta previa, abnormal amniotic fluid), and twin or embryo transplantation pregnancy. The clinical data of LPIs and EPIs were comparatively studied.

The laboratory test results were prospectively studied and complications of PIs admitted into the present department included: blood chemistry, perinatal complications (including jaundice, hypothermia, hypoglycemia, transient tachypnea, breathing distress, apnea, feeding intolerance), assisted ventilation (including non-invasive ventilation), and other indicators. Feeding intolerance referred to one of the following: frequent vomiting (≥ three times/day), milk amount non-increasing or decreasing (> three days), gastric retention (retention capacity >1/3 of previous feedings) [11]; The clinical data and laboratory tests of LPIs and EPIs were comparatively studied. One hour after PIs admitted into the present department, radial artery blood was sampled under aseptic conditions for biochemical blood tests and blood routine tests. The diagnostic criteria of other complications were referred by "practical neonatology", fourth edition [12].

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Table 1. — *Comparison of preterm indicators [n (%)].*

Obstetric indicator	EPIs (n=154)	LPIs (n=407)	χ^2	*p*
Twin	24 (15.58)	58 (14.25)	0.16	>0.05
C-section	63 (40.91)	196 (48.16)	2.36	>0.05
Asphyxia at birth	68 (44.16)	37 (9.09)	90.30	<0.01
Maternal hypertension	10 (6.49)	43 (10.57)	2.17	>0.05
Maternal anemia	6 (3.90)	6 (1.47)	2.08	>0.05
Maternal diabetics	5 (3.25)	6 (1.47)	1.02	>0.05
Maternal cholestasis	11 (7.14)	32 (7.86)	0.08	>0.05
Placental abruption	38 (24.68)	131 (32.19)	2.99	>0.05
Placental peeling	12 (7.79)	7 (1.72)	12.59	<0.01
Placenta previa	29 (18.83)	15 (3.69)	35.46	<0.01
Abnormal amniotic fluid	24 (15.58)	42 (10.32)	2.98	>0.05
Embryo transplantation pregnancy	10 (6.49)	19 (4.67)	0.76	>0.05

Table 2. — *Comparison of blood biochemistry (±s).*

Blood biochemistry	EPIs (n=154)	LPIs (n=407)	χ^2	*p*
Albumin (g/L)	33.72±4.40	35.92±3.06	6.68	<0.01
Globulin (g/L)	14.31±3.57	15.39±4.34	2.76	<0.01
Total bilirubin (μmol/L)	12.38±9.54	13.12±11.59	0.71	>0.05
Triglycerides (mmol/L)	0.45±0.49	0.62±0.46	3.84	<0.01
Total cholesterol (mmol/L)	2.46±0.72	2.32±0.81	1.88	>0.05
Total calcium (mmol/L)	2.23±0.19	2.25±0.23	0.96	>0.05
Serum phosphorus (mmol/L)	1.88±0.52	2.17±0.58	5.43	<0.01
Serum iron (umol/L)	14.52±6.19	17.62±7.99	4.35	<0.01
Hemoglobin (g/L)	162.85±22.13	170.28±20.83	3.71	<0.01

Table 3. — *Comparison of birth complications [n (%)].*

Complication	EPIs (n=154)	LPIs (n=407)	χ^2	*p*
Jaundice	144 (93.51)	366 (89.93)	1.73	>0.05
Hypothermia	27 (17.53)	21 (5.16)	21.86	<0.01
Hypoglycemia	34 (22.08)	47 (11.55)	10.03	<0.01
Transient tachypnea	31 (20.13)	97 (23.83)	0.87	>0.05
Respiratory distress	50 (32.47)	22 (5.41)	73.14	<0.01
Apnea	57 (37.01)	28 (6.88)	78.91	<0.01
Feeding intolerance	46 (29.87)	20 (4.91)	67.03	<0.01
Assisted ventilation	45 (29.22)	19 (4.67)	66.64	<0.01

Statistical analysis

SPSS 13.0 was used. The counting data were assessed by chi-square test or corrected chi-square test; the measurement data were expressed as mean ± standard error (x ± s), and the *t*-test was also performed, with a $p < 0.05$ considered as statistically significant.

Results

Basic conditions

The EPIs group included 86 males (55.84%) and 68 females (44.16%), with gestational age of 30.47 ±1.52 weeks, birth weight as 1,702.62 ± 494.93 grams. The LPIs group included 252 males (61.92%) and 155 females (38.08%), with gestational age of 35.23 ±0.94 weeks, and birth weight was 2,707.07 ± 473.66) grams. The gender ratio showed no statistical significance between the two groups ($\chi^2 = 1.72$, $p > 0.05$); the gestational age and birth weight of the EPIs group was significantly lower than the LPIs group, and the difference was statistically significant ($t = 44.57$, 22.14, $p < 0.01$).

The incidence rates of asphyxia at birth, placental abruption, and placenta previa in the EPIs group were significantly higher than the LPIs group, and the differences were statistically significant ($p < 0.01$, Table 1). Albumin, globulin, triglycerides, serum phosphorus, serum iron, and hemoglobin level in the EPIs group were significantly lower than the LPIs group, and the differences were statistically significant ($p < 0.01$, Table 2). Hypothermia, hypoglycemia, respiratory distress, apnea, feeding intolerance, and assisted ventilation rate in the EPIs group were significantly higher than the LPIs group, and the differences were statistically significant ($p < 0.01$, Table 3).

Discussion

Overview of preterm birth

Preterm birth was a leading cause of neonatal death and long-term neurological sequelae. In the past ten years, the preterm birth rate has increased by 33% in USA from 1981 to 2006, and the mortality rate was higher [2], among which LPIs accounted for 70% of all PIs, and the increased birth rate of LPIs was the main reason of the increasing of PIs [13]. The data showed that LPIs accounted for 72.55% of all PIs, and a survey of birth status in urban China in 2005 showed that PIs with gestational age as 32 to 36 weeks, accounted for 85.2% of all PIs [14]. The recent increasing of PIs had several reasons, among which the frequently reported ones included maternal demographic changes (such as late childbearing), infertility treatment, increased maternal age, multiple pregnancy, and pregnancy-concomitant diseases, especially obesity [15, 16]. The statistics confirmed that maternal chorioamnionitis, high blood pressure, and premature rupture of membranes could cause later preterm birth [17]. The previous history of premature birth, too short interval between two pregnancies (<12 months), and bleeding in early pregnancy increased the risk of preterm birth [17].

Features of PIs after delivery

1) Appearance included relatively large head, accounting for one-third of body, wider fontanelle, softer skull and nails, fluffy hair, undescended or non-fully descended testes in males, the labium minus pudenda was not covered by labium major pudenda in females. 2) Thermoregulation included: lacking mature development of body temperature center, less subcutaneous fats, while larger surface area, less muscle activities and autologous heat production, and

with easy body heat loss. Therefore, under normal circumstances, the body temperature would decrease in lower ambient cold conditions, which might even cause intracranial hemorrhage in severe cases. 3) Nervous system included poorer nerve reflexes and the infant would usually be in the sleeping state. If the body weight was 1,500 grams or less, infants would also be prone to intracranial hemorrhage, requiring extensive clinical attention. 4) Immune functions, compared with the full-term infants, PIs had poorer immune function lacking adequate anti-scavenging abilities against bacteria and viruses, and could only acquire less immunoglobulins from mother. Because they had weak resistance to infections, therefore, they were prone to sepsis, which might ultimately enhance the mortality rate to a larger extent.

Predisposing factor analysis of EPIs and LPIs

The risk factors of preterm birth reported included threatened eclampsia, placental abruption, intrauterine fetal growth restriction, and other adverse signs, oligohydramnios, pre-pregnancy diabetes and gestational diabetes, and abnormal fetal heart rate, etc; however, 6.1%~23.2% of PI showed no preterm signs [1]. The data of this study showed that the gender ratio between the two groups showed no statistically significant difference (χ^2=1.72, $p > 0.05$), gestational age and birth weight of EPIs were significantly lower than LPIs, and the differences were statistically significant (t = 44.57, 22.14, $p < 0.01$), the incidence rates of asphyxia at birth, placental abruption, and placenta previa of EPIs were significantly higher than LPIs, and the differences were statistically significant ($p < 0.01$), indicating that placenta previa and placental abruption were the unique risk factors for EPIs. Therefore, high-risk factors for EPIs should be especially considered, to reduce the incidence rate of LPIs, which is also significant to reduce neonatal mortality.

Effects of preterm birth on biochemical indicators of EPIs and LPIs

In order to improve the chances of survival, EPIs would have a series of adaptive changes in utero, including intrauterine growth and metabolism. After delivery, detached from the adverse intrauterine environments, growth and metabolism of EPIs would be different from LPIs. The total protein in EPIs could sensitively react to the changes of nutritional status and it was the important indicator to evaluate the nutritional status and detect the effects of nutritional support internationally [18]. The data showed that the levels of albumin, globulin, triglycerides, serum phosphorus, serum iron, and hemoglobin in EPIs were significantly lower than LPIs, and the differences were statistically significant ($p < 0.01$), indicating that EPIs would be more prone to anemia, infections, and other diseases, so a more active and reasonable nutritional support would be required.

Effects of preterm birth on complications of EPIs and LPIs

Foreign large numbers of clinical studies have found that the common clinical problems in PIs included NRDS, neonatal transient dyspnea, hyperbilirubinemia, feeding difficulties, and low blood sugar, and among which the most common was respiratory diseases [19]. The data showed that hypothermia, hypoglycemia, respiratory distress, apnea, feeding intolerance, and assisted ventilation rate in EPIs were significantly higher than LPIs, and the differences were statistically significant ($p < 0.01$), consistent with the fact that respiratory distress was the most prominent clinical problem. In addition, placenta previa, placental abruption, as well as such intrauterine fetal blood loss due to fetal maternal blood transfusion and twin blood transfusion, could cause fetal anemia, maternal hypertension, and other vascular diseases, thus resulting in small fetal development, hypoxia, etc., which required more clinic attention [19].

In conclusion, LPIs accounted for the majority of PIs, and placental abruption and placenta previa were the unique risk factors in EPIs. EPIs had lower nutritional reserves than LPIs and would be more susceptible to perinatal complications.

References

[1] Loftin R.W., Habli M., Snyder C.C., Cormier C.M., Lewis D.F., Defranco E.A.: "Late preterm birth". *Rev. Obstet. Gynecol*., 2010, *3*, 10.

[2] Raju T.N., Higgins R.D., Stark A.R., Leveno K.J.: "Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development". *Pediatrics*., 2006, *118*, 1207.

[3] Platt M.J., Cans C., Johnson A., Surman G., Topp M., Torrioli M.G., *et al.:* "Trends in cerebral palsy among infants of very low birthweight (<1500 g) or born prematurely (<32 weeks) in 16 European centres: a database study". *Lancet*, 2007, *369*, 43.

[4] Engle W.A.: "A recommendation for the definition of "late preterm" (near term) and the birth weight system". *Semin. Perinatol*., 2006, *30*, 2.

[5] Lee S.K., McMillan D.D., Ohlsson A., Pendray M., Synnes A., Whyte R., *et al.:* "Variations in practice and outcomes inthe Canadian NICU: 1996-1997". *Pediatrics*, 2000, *105*, 1070.

[6] Claas M.J., Bruinse H.W., van der Heide-Jalving M., Termote J.U., de Vries L.S.: "Changes in survival and neonatal morbidity in infants with a birth weight of 750g or less". *Neonatology*, 2010, *98*, 278.

[7] Wilson-Costello D., Friedman H., Minich N., Fanaroff A.A., Hack M.: "Survival rates with increased neurodevelopmental disability for extremely low birth weight infants in the 1990s". *Pediatrics*, 2005, *115*, 997.

[8] Marrocchella S., Sestilli V., Indraccolo U., de Rosario F., Castellana L., Mastricci A.L., *et al.:* "Late preterm births: a retrospective analysis of the morbidity risk stratified for gestational age". *Springerplus*, 2014, *3*, 114.

[9] Reichman N.E., Teitler J.O., Moullin S., Ostfeld B.M., Hegyi T.: "Late-preterm birth and neonatal morbidities: population-level and within-family estimates". *Ann. Epidemiol*., 2015, *25*, 126.

[10] Kitsommart R., Phatihattakorn C., Pornladnun P., Paes B.: "A prospective study of the severity of early respiratory distress in late preterms compared to term infants". *J. Matern. Fetal Neonatal Med*., 2014, *24*, 1.

[11] Wagner J., Hanson C., Anderson-Berry A.: "Considerations in meeting protein needs of the human milk-fed preterm infant". *Adv. Neonatal Care*, 2014, *14*, 281.
[12] Shao X.M., Ye H.M., Qiu X.X.: "Practical neonatology". 4th ed. Beijing: People's Health Publishing House, 2012, 59.
[13] Shapiro-Mendoza C.K., Lackritz E.M.: "Epidemiology of late and moderate pretermbirth. Semin". *Fetal Neonatal Med*., 2012, *17*, 120.
[14] Li J., Wang Q.H., Wu H.M., Wei K.L., Yang Y.J., DU L.Z., *et al.:* "A survey of neonatal births in maternity departments in urban China in 2005". *Zhongguo Dang Dai Er Ke Za Zhi*, 2012, *14*, 7.
[15] Martin J.A., Hamilton B.E., Sutton P.D., Ventura S.J., Mathews T.J., Kirmeyer S., *et al.:* "Births: final data for 2007". *Natl. Vital. Stat. Rep*., 2010, *58*, 1.
[16] Eagle W.A.: "Morbidity and mortality in late preterm and early term newborns:a continuum". *Clin. Perinatol*., 2011, *38*, 493.
[17] Selo-Ojeme D.O., Tewari R.: "Late preterm (32-36 weeks) birth in a North London hospital". *J. Obstet. Gynaecol*., 2006, *26*, 624.
[18] Zecca E., Costa S., Barone G., Giordano L., Zecca C., Maggio L.: "Proactive enteral nutrition in moderately preterm small for gestationalage infants: a randomized clinical trial". *J. Pediatr*., 2014, *165*, 1135.
[19] Wang M.L., Dorer D.J., Fleming M.P., Catlin E.A.: "Clinical outcomes of near-term infants". *Pediatrics*, 2004, *114*, 372.

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