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Sex-Specific Risk Factors and Organ Injury Patterns in Neonates: A Comprehensive Analysis of Clinical and Maternal Factors

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Abstract:

Background: Neonatal organ injuries significantly exacerbate the burden of neonatal death and disability. This study investigates sex-specific risk factors and patterns of neonatal organ injuries, taking into account both clinical and maternal factors. **Methods:** We conducted a retrospective analysis of 155 mother-infant pairs admitted to Sichuan Provincial Maternity and Child Health Hospital (2020-2022). Univariate and multivariate analyses, including restricted cubic spline models, were performed to identify risk factors. Sex-specific subgroup analyses and correlation studies of organ injuries were also conducted. **Results:** Key results revealed distinct sex-based predictors. For male neonates, gestational age (OR=1.41, 95% CI: 1.13-1.87, P=0.007) and birth weight (OR=1.00, 95% CI: 1.00-1.00, P=0.008) were significantly associated with organ injury risk. For female neonates, initial C-reactive protein levels showed a significant association (OR=1.14, 95% CI: 1.01-1.31, P=0.045). Strong correlations were found between various types of brain injuries, with cerebral infarction showing high co-occurrence with hemorrhagic injuries (OR range: 60.77-117.81, P<0.001). **Conclusion:** Our findings highlight the importance of sex-specific approaches in neonatal care and risk assessment. The complex interplay between different organ injuries, particularly in the brain, underscores the need for comprehensive monitoring strategies in neonatal intensive care units. These results provide a foundation for developing targeted preventive measures and individualized care protocols.

Keywords: Neonatal organ injury, Sex-specific risk factors, Cerebral infarction, Intracranial hemorrhage, Maternal factors

Introduction

Neonatal health remains a critical global public health priority. According to reports from the United Nations, while neonatal mortality has declined in recent decades, preventable deaths persist with 2.3 million neonates lost globally in 2022 [1]. United Nations Sustainable Development Goal 3.2 specifically calls for the elimination of preventable deaths among neonates and children under five years of age [2]. Many countries are working toward this goal by optimizing healthcare systems, expanding interventions, and addressing regional inequalities [3]. Beyond survival rates, attention must also be given to the quality of survival. According to the Global Burden of Disease 2021, neonatal diseases contributed to 186 million disability-adjusted life years, placing a heavy burden on families and society [4],[5]. While advances in high-risk pregnancy perinatal management and neonatal intensive care have improved neonatal survival rates, the growing burden of disability remains a pressing concern [3]-[5]. Therefore, improving neonatal health and refining neonatal care strategies are crucial for addressing adverse neonatal outcomes.

The neonatal period is features unique vulnerabilities with marked by imperfect development of various systems, subtle clinical manifestations, and rapid disease progression after falling ill [6]-[8]. However, Organ systems lack adult-like stability, evolving dynamically from minutes to months postpartum, creating critical windows for injury susceptibility [6],[9]-[11]. Mounting evidence confirms sex-specific pathophysiology in terms of physiological structure, metabolic function, and susceptibility to diseases [9]-[11]. For example, fetal sex significantly affects the developing alveolar structure, surfactant synthesis, and Na^+ transport, which may influence the tolerance to organ injury [10]. Clinically, male neonates are more prone to respiratory distress syndrome and bronchopulmonary dysplasia compared to female neonates [10]. The sexual dimorphism in gene expression and the regulation of sex hormone levels during embryonic development may partly explain the potential link between gender differences and the risk of organ damage [12],[13]. Therefore, understanding gender differences is crucial for the prevention and management of neonatal organ injury.

For many years, numerous scholars have focused on exploring the risk factors associated with neonatal diseases, with the goal of identifying effective prevention and intervention measures to improve care strategies. Despite growing recognition of sex differences, systematic investigations into sex-specific risk factors for neonatal organ injury remain limited. Additionally, the co-occurrence patterns of multiple organ injuries-particularly within the brain, a common site of neonatal damage-are poorly characterized. In light of this, the study is to conduct a comprehensive analysis of 155 mother-infant pairs to identify sex-specific risk factors (including clinical, maternal, and biochemical variables) associated with neonatal organ injury and characterize the co-occurrence patterns of different organ

injuries. We sought to provide evidence for developing sex-tailored risk assessment tools, personalized preventive measures, and comprehensive neonatal intensive care monitoring protocols to improve neonatal health outcomes.

Materials and Methods

Study Design and Population

The data for this study were selected from mother-infant pairs who delivered at Sichuan Provincial Maternal and Child Health Care Hospital and had their neonates hospitalized between Jan. 2020 and Dec. 2022. A total of 155 mother-infant pairs were included in the sample. This retrospective study included all eligible mother-infant pairs who received treatment at the hospital during the specified time period. Exclusion criteria were severe congenital malformations and incomplete medical records.

Data Collection

We collected detailed clinical and demographic data from the hospital's electronic medical records system. The information gathered included neonatal characteristics (such as gender, birth weight, gestational age, Apgar score), maternal factors (age, pregnancy complications, mode of delivery), laboratory test results, and clinical treatment parameters.

Definition of Organ Injuries

The definition of organ injury was based on clinical diagnoses and imaging results. Intracranial hemorrhage (ICH), subdural hemorrhage (SDH), subarachnoid hemorrhage (SAH), parenchymal brain hemorrhage, and cerebral infarction were diagnosed through cranial ultrasound or MRI. Sepsis and central nervous system (CNS) infections were diagnosed based on clinical manifestations and laboratory test results. Retinopathy was determined through fundus examination.

Analysis of Organ Injury Associations

To explore the associations between different organ injuries, we conducted pairwise analyses of various organ injuries. Fisher’s exact test was used to calculate conditional probabilities, odds ratios (ORs), and their 95% confidence intervals (CIs), along with statistical significance tests. We converted ICH and retinopathy of prematurity (ROP) into binary variables for consistent comparison with other binary injury variables.

Correlation Analysis of Organ Injuries

To further investigate the associations between different organ injuries, we conducted correlation analyses for six major neonatal organ injuries. These injuries included SDH, SAH, parenchymal brain hemorrhage, cerebral infarction, sepsis, and CNS infections. The Pearson correlation coefficient was calculated using the cor() function in R, and the corresponding p-values were determined using the cor.test() function. To visually present the results, we used the corrplot package to create a heatmap.

Statistical Analysis of Risk Factors for Neonatal Organ Injury

This study employed comprehensive statistical analysis methods to assess the risk factors for neonatal organ injuries. First, we conducted univariate analysis, selecting appropriate statistical methods for continuous variables based on their distribution characteristics. For normally distributed variables, we used independent samples t-tests; for non-normally distributed variables, we applied the Wilcoxon rank-sum test. To visually demonstrate the association between each factor and the risk of organ injury, we constructed forest plots displaying the OR and its 95% CI for each variable. For those variables that showed significant associations ($P<0.05$) in the univariate analysis, we further performed restricted cubic spline (RCS) analysis to explore potential nonlinear relationships between these factors and the risk of organ injury. The RCS analysis used four knots, with logistic regression modeling for fitting. We computed the chi-square statistics, overall association p-value, nonlinear association p-value, and model goodness-of-fit (R^2) for each model. Additionally, we plotted RCS curves to visually represent the dose-response relationship between each factor and the risk of organ injury.

Sex-specific Subgroup Analysis

We conducted gender-specific subgroup analyses of risk factors for neonatal organ injuries. The analysis included 20 continuous variables, covering neonatal characteristics (such as age, birth weight, and gestational age), Apgar score, maternal factors, laboratory test results (e.g., white blood cell count, platelet count, C-reactive protein, procalcitonin), and clinical treatment parameters (e.g., ventilation time, antibiotic use duration). For each continuous variable, we performed logistic regression analysis separately for male and female neonates to assess its association with the risk of organ injury. To ensure the reliability of the statistical analysis, we only included subgroups with a sample size of at least 10. We calculated the OR and its 95% CI for each factor and assessed statistical significance using the Wald test. To evaluate the moderating effect of gender on risk factors, we conducted interaction effect analysis on the full sample, where gender

was treated as a categorical variable interacting with each continuous variable. The significance of interaction effects was determined based on the P-value of the interaction term in the logistic regression model.

Statistical Analysis

All statistical analyses were performed using R software (version 4.3.1). We utilized the dplyr, tidyr, and broom packages for data processing and statistical analysis, and used the ggplot2 package to create forest plots for visualizing the results. The forest plots display the OR and its 95% CI for each factor in the male and female subgroups, along with P-values and sample sizes. For results where the OR or the upper limit of the CI exceeded 2, we marked these values distinctly on the plot and included the actual values to ensure a comprehensive presentation of the data.

Results

Demographic and Clinical Characteristics of the Study Population

A total of 155 neonates were included in the study, with 82 males (52.9%) and 73 females (47.1%) (Table 1). The median postnatal age at birth was 0 days (interquartile range (IQR): 0-4 days), the median birth weight was 2,315 g (IQR: 1,847.5-2,650 g), and the median gestational age was 35 weeks (IQR: 33-36 weeks). Cesarean section was the primary mode of delivery, accounting for 73.5% (114 cases). The median maternal age was 30 years (IQR: 28-33 years). Notably, 65.8% (102 cases) of mothers had chorioamnionitis, and 75.5% (117 cases) had pregnancy complications. Regarding neonatal organ injuries, 78.7% (122 cases) had no ICH, with 18.1% (28 cases) grade 1 and 3.2% (5 cases) grade 2. SDH and SAH each occurred in 44.5% (69 cases). Periventricular leukomalacia (PVL) and cerebral infarction each occurred in 62.6% (97 cases). The majority of neonates (94.2%, 146 cases) did not undergo surgical intervention. In terms of complications, 13.5% (21 cases) had sepsis, and 5.8% (9 cases) had CNS infections. Regarding ROP, 54.8% (85 cases) were classified as stage 0, 11.0% (17 cases) as stage 1, and 34.2% (53 cases) as stage 2.

Table 1 Baseline Characteristics of Neonates and Maternal Factors

Characteristics	Level	Overall (n =155)	Characteristics	Level	Overall (n =155)
sex	Male	82 (52.9)	SDH	Yes	69 (44.5)
	Female	73 (47.1)		No	86 (55.5)
Age (days)		0.00 [0.00, 4.00]	SAH	Yes	69 (44.5)
Birth weight (g)		2,315.00 [1,847.50, 2,650.00]		No	86 (55.5)
Gestational age (weeks)		35.00 [33.00, 36.00]	Cerebral hemorrhage	Yes	67 (43.2)
Maternal age (years)		30.00 [28.00, 33.00]		No	88 (56.8)
WBC at admission		9.98 [8.30, 12.84]	Other hemorrhage	Yes	60 (38.7)
WBC at follow-up		11.71 [9.03, 15.09]		No	95 (61.3)
PLT at admission		255.00 [212.50, 311.00]	PVL	Yes	97 (62.6)
PLT at follow-up		253.00 [194.50, 311.00]		No	58 (37.4)
CRP at admission		4.00 [2.44, 8.46]	Cerebral infarction	Yes	97 (62.6)
CRP at follow-up		3.20 [1.24, 8.00]		No	58 (37.4)
Delivery mode	Vaginal	41 (26.5)	surgery	Yes	9 (5.8)
	Cesarean	114 (73.5)		No	146 (94.2)
Maternal infection	Yes	102 (65.8)	sepsis	Yes	21 (13.5)
	No	53 (34.2)		No	134 (86.5)
Pregnancy complications	Yes	117 (75.5)	CNS infection	Yes	9 (5.8)
	No	38 (24.5)		No	146 (94.2)
ICH grade	0	122 (78.7)	ROP stage	0	85 (54.8)
	1	28 (18.1)		1	17 (11.0)
	2	5 (3.2)		2	53 (34.2)

Note: Values are presented as median [interquartile range] for continuous variables and number (percentage) for categorical variables. Abbreviation: Interquartile range, IQR; white blood cell, WBC; platelet, PLT; C-reactive protein, CRP; intracranial hemorrhage, ICH; subdural hemorrhage, SDH; subarachnoid hemorrhage, SAH; periventricular leukomalacia, PVL; sepsis and central nervous system, CNS; Retinopathy of prematurity, ROP.

Patterns and Correlations of Organ Injury Co-occurrence in Neonates

Further analysis results revealed a complex and significant association pattern among neonatal organ injuries (Figure 1). There was a strong positive correlation among cerebrovascular-related injuries. The correlation coefficients between cerebral infarction and the other three types of hemorrhagic injuries (SDH, SAH, and parenchymal hemorrhage) all exceeded 0.6 (r value range: 0.638-0.648, $P < 0.001$). There was a strong correlation between cerebral hemorrhage and SDH (OR = 7.93, 95% CI: 3.69-17.74, $P < 0.001$), and 77.9% of patients with SDH also had

cerebral hemorrhage. The association between cerebral hemorrhage and SAH was even more significant (OR = 19.67, 95% CI: 8.30-50.21, P < 0.001), and 84.9% of patients with SAH also had cerebral hemorrhage. There was also a strong positive correlation between these two injuries (r = 0.633, P < 0.001). Cerebral infarction showed an extremely strong association with both SDH and SAH (OR = 60.77, 95% CI: 14.45-546.37, P < 0.001). Among patients with these two types of hemorrhages, the incidence of cerebral infarction was 65.1%. In addition, there was an extremely high comorbidity rate between cerebral hemorrhage and cerebral infarction. 98.3% of patients with cerebral infarction also had cerebral hemorrhage (OR = 117.81, 95% CI: 18.52-4799.84, P < 0.001). It is worth noting that there was an extremely strong correlation between CNS infection and sepsis (OR = 76.89, 95% CI: 9.22-3567.31, P < 0.001). Among patients with sepsis, the incidence of CNS infection was as high as 99.3%, and there was also a moderate positive correlation between these two injuries (r = 0.547, P < 0.001). However, the correlation between sepsis and other types of organ injuries was weak or not significant, which may imply the unique pathological processes of different types of organ injuries.

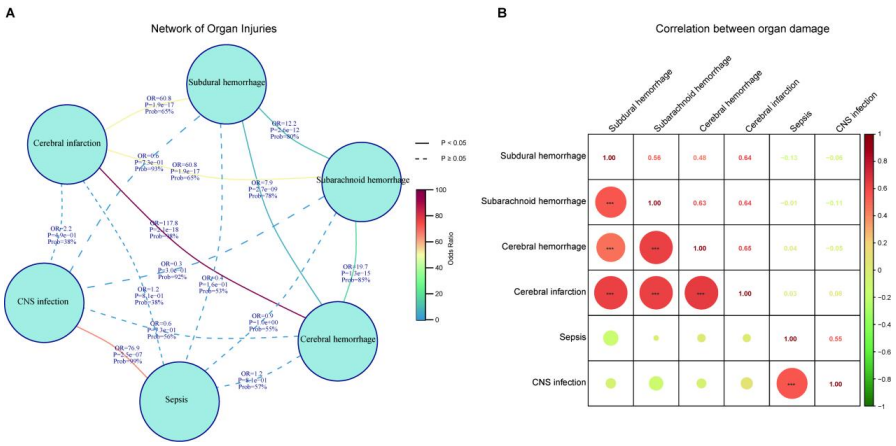

Figure 1 Network and Correlation Analysis of Organ Injuries in Neonates.

A: Network of associations between different types of organ injuries. B: Correlation matrix of organ injuries, where the lower triangle displayed significance levels and the upper triangle displayed correlation coefficients.*P < 0.05, **P < 0.01, and ***P < 0.001.

Univariate Analysis of Risk Factors for Organ Injuries in Neonates

The results of univariate analysis show that multiple factors are associated with the risk of neonatal organ injury (Figure 2A and Table 2). Birth weight (OR = 1.66, 95% CI: 1.14-2.43, P = 0.01) and gestational age (OR = 1.71, 95% CI: 1.12-2.59,

P< 0.05) are two significant risk factors, both associated with an increased risk of organ injury . Although the 1-minute Apgar score (OR = 1.44, 95% CI: 0.89-2.31, P > 0.05) and the 10-minute Apgar score (OR = 1.34, 95% CI: 0.89-2.01, P = 0.10) did not reach statistical significance, they also showed a trend of increasing the risk of organ injury. Other factors such as age, maternal age, time of membrane rupture, hematological indices (WBC, PLT, CRP), PCT, mode of respiratory support, antibiotic use, weight gain rate, and full enteral feeding time did not show significant correlations in the univariate analysis.

Further RCS analysis explored the nonlinear relationships between birth weight and gestational age, the two significant factors (Figure 2B). The results showed a significant overall association between birth weight and the risk of organ injury (χ^2 = 11.89, P = 0.02), but no significant nonlinear relationship (P = 0.13), explaining 10.4% of the risk variation. The relationship between gestational age and the risk of organ injury was more complex; there was a significant overall association (χ^2 = 15.04, P = 0.01), and a significant nonlinear relationship was found (P = 0.03), explaining 13.1% of the risk variation. These findings suggest that the effect of gestational age on the risk of organ injury may not be a simple linear relationship but could involve a critical threshold or a more complex curve, providing more refined guidance for risk assessment in clinical practice.

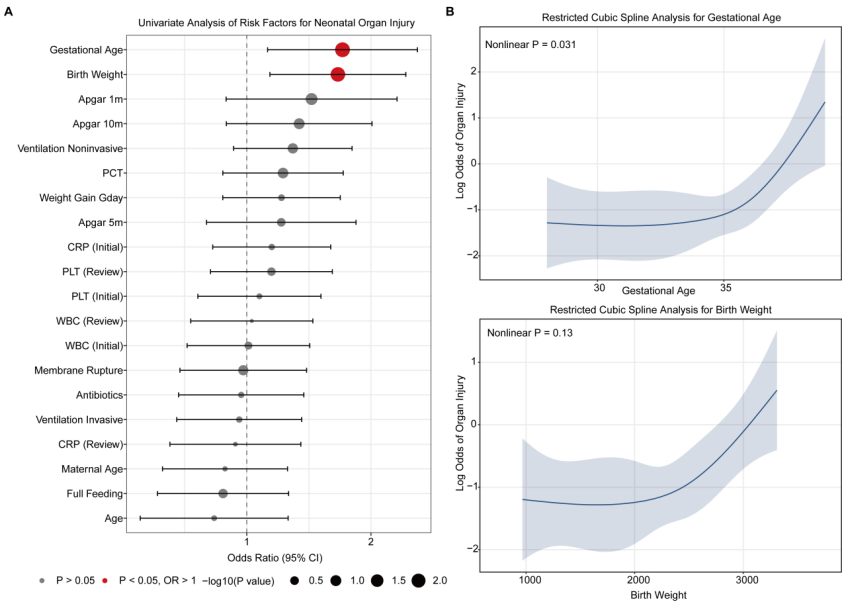

Figure 2 Risk Factor Analysis for Neonatal Organ Injuries.

A: Univariate analysis of risk factors for organ injuries in Neonates. B: Restricted cubic spline analysis of significant factors from univariate analysis.

Table 2 Univariate Analysis of Risk Factors for Organ Injuries in Neonates

Variable	OR	CI lower	CI upper	P value	Variable	OR	CI lower	CI upper	P value
Age	0.83	0.55	1.26	0.74	WBC (Initial)	1.01	0.72	1.42	0.42
Birth weight	1.66	1.14	2.43	0.01	PLT (Initial)	1.07	0.76	1.51	0.73
Gestational age	1.71	1.12	2.59	0.0	CRP (Initial)	1.15	0.83	1.60	0.66
Apgar 1m	1.44	0.89	2.31	0.05	WBC (Review)	1.03	0.73	1.45	0.86
Apgar 5m	1.21	0.8	1.84	0.33	PLT (Review)	1.15	0.82	1.61	0.34
Apgar 10m	1.34	0.89	2.01	0.10	CRP (Review)	0.94	0.65	1.35	0.83
Maternal age	0.89	0.62	1.26	0.79	PCT	1.22	0.87	1.71	0.12
Membrane rupture	0.98	0.69	1.40	0.15	Antibiotics	0.97	0.68	1.37	0.68
Ventilation Invasive	0.96	0.68	1.36	0.66	Weight Gain Gday	1.21	0.87	1.68	0.61
Ventilation Noninvasive	1.29	0.93	1.80	0.14	Full Feeding	0.88	0.61	1.26	0.23

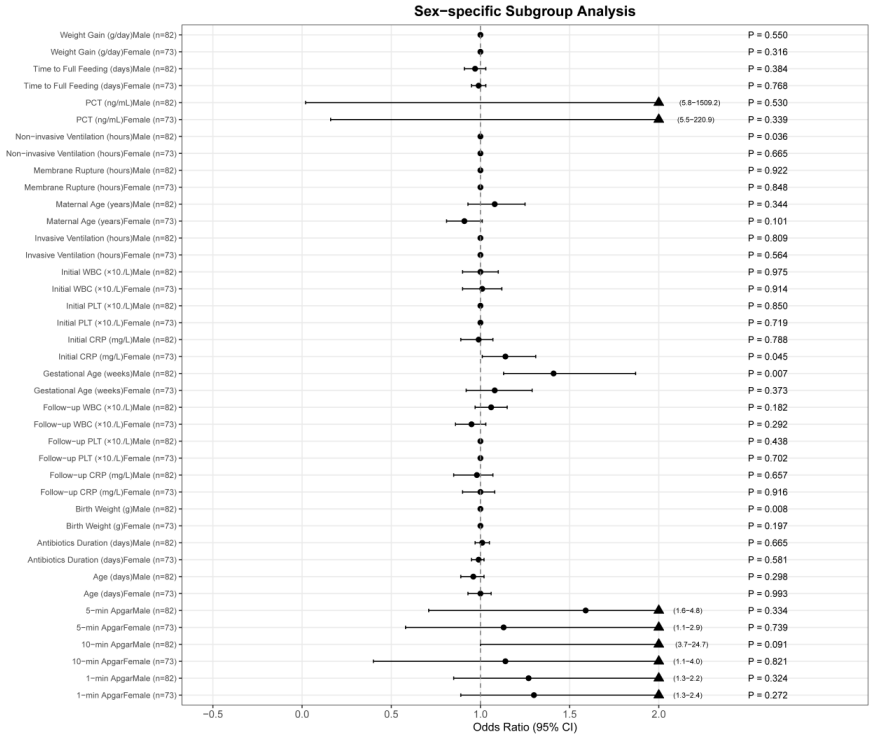

Figure 3 Subgroup Analysis of Risk Factors for Neonatal Organ Injury by Sex

Subgroup Analysis of Risk Factors for Neonatal Organ Injury by Sex

The gender subgroup analysis revealed differences in neonatal organ injury risk factors between male and female infants (Figure 3, Table S1). In male neonates, birth weight (OR = 1.00, 95% CI: 1.00-1.00, P = 0.008) and gestational age (OR = 1.41, 95% CI: 1.13-1.87, P = 0.007) were significantly associated with the risk of organ injury. Notably, for each additional week of gestational age, the risk of organ injury in male infants increased by 41%. Additionally, non-invasive ventilation time was also significantly associated with organ injury risk in male neonates (OR = 1.00, 95% CI: 1.00-1.00, P = 0.036), although the effect size was small. In contrast, the risk factor pattern for female neonates differed. The initial C-reactive protein level was the only factor in female infants that showed statistical significance (OR = 1.14, 95% CI: 1.01-1.31, P = 0.045), indicating that for every 1 mg/L increase in CRP, the risk of organ injury increased by 14%. It is worth noting that certain factors showed potential importance in both genders, even though they did not reach statistical significance. For instance, the 10-minute Apgar score was associated with an increased risk of organ injury in male neonates (OR = 3.74, 95% CI: 1.00-24.66, P = 0.091), while this association was not evident in female infants.

Discussion

Neonatal organ injuries exacerbate the burden of neonatal death and disability. Therefore, this study comprehensively analyzed various data of 155 mother-infant pairs to identify the risk factors for neonatal organ injuries. The research findings demonstrate the complex associations between neonatal organ injuries and related influencing factors, and reveal the gender-specific risk factors for neonatal organ injuries.

From the results of univariate analysis, birth weight and gestational age were identified as significant risk factors for neonatal organ injuries, which is highly consistent with a large number of previous studies. Preterm infants and low-birth-weight infants face a higher risk of injury in the extra-uterine environment due to incomplete organ development [14],[15]. A lower Apgar score is associated with a relatively higher risk of neonatal death [16]. Although the 1-minute and 10-minute Apgar scores in our results did not reach statistical significance, they showed a trend of increased risk. This suggests that even if the scores are within the normal range, neonates may have potential health risks and should be closely monitored. In the restricted cubic spline analysis of birth weight and gestational age, a significant overall association was found between birth weight and the risk of organ injury, but the non-linear relationship was not significant. This indicates that the relationship between them is relatively straightforward, with the lower the birth weight, the higher the risk. In contrast, the relationship between gestational age and the risk of organ injury is more complex. Not only is there a significant overall association, but also a significant non-linear relationship. This means that at different gestational

age stages, the mechanisms and influencing factors of organ injury vary greatly. For example, extremely preterm infants, due to the severe lag in the development of multiple organ systems, face different types and degrees of injury risks compared with late preterm infants, and their survival rate is also lower [17].

The gender subgroup analysis further revealed gender differences in the risk factors for neonatal organ injuries. Among male neonates, birth weight, gestational age, and the duration of non-invasive ventilation were significantly associated with the risk of organ injury. Epidemiological studies have also shown that male fetuses have a higher incidence of preterm birth [18],[19]. The significant correlation between the duration of non-invasive ventilation and organ injury in male infants reflects the differences in the respiratory systems of male and female infants. Male neonates, especially preterm infants, often exhibit a significant "male disadvantage" in lung development. Previous studies have shown that male infants are more prone to conditions such as poor lung organ development [10],[18]. The 10-minute Apgar score in male infants also showed an association with an increased risk of organ injury. Although it did not reach statistical significance, a low Apgar score to some extent reflects the condition of the neonatal respiratory system, and also indirectly reflects the developmental differences in the respiratory systems of males and females. For female neonates, the initial C-reactive protein level is the only statistically significant risk factor. For every 1 mg/L increase, the risk of organ injury increases by 14%. The initial C-reactive protein is a biomarker for the early detection of acute infections and inflammation [20]. This highlights the crucial role of the inflammatory response in female neonatal organ injuries, and the expression of the initial C-reactive protein in the inflammatory response in female infants may be more sensitive. In several other studies, males tend to exhibit a higher inflammatory response [21][23], which may be related to the gender differences in immune system regulators between males and females [24]. These results suggest that clinically, male infants with preterm birth and low birth weight may require closer monitoring than female infants, while for female infants, the level of initial inflammatory markers may be a more important risk indicator.

In the study of the association patterns of neonatal organ injuries, an extremely strong correlation was demonstrated between CNS infections and sepsis. Especially among septic patients, the incidence of CNS infections was as high as 99.3%. This indicates a close causal relationship between the two, possibly because the systemic inflammatory response disrupts the integrity of the blood-brain barrier, increasing the risk of CNS infections [25]. Among our study subjects, 65.8% of the mothers had chorioamnionitis, and chorioamnionitis increases the likelihood of early neonatal sepsis [26]. Clinically, postpartum and intrauterine infections can be controlled through maternal preventive measures to prevent and limit neonatal sepsis, thereby reducing neonatal organ injuries, especially CNS infections [27]. Regarding cerebrovascular injuries, the proportion of children with cerebrovascular injuries

was extremely high, which is related to the fact that most neonates are preterm infants. Meanwhile, there were also complex and close relationships among cerebrovascular-related injuries. The correlation coefficients between cerebral infarction and SDH, SAH, and parenchymal hemorrhage all exceeded 0.6, which is consistent with the studies of Cain et al. [28] and Assis et al. [29], cerebral infarction is usually accompanied by bleeding. On the other hand, intraventricular hemorrhage can also transform into hemorrhagic infarction [30]. In addition, there was a strong correlation between cerebral hemorrhage and SDH, as well as SAH. This suggests that there may be a common pathophysiological basis among cerebrovascular injuries, such as immature blood vessel wall development, hemodynamic disorders, genetic factors, etc. [31]-[33]. These factors may simultaneously affect the cerebrovascular vessels in multiple locations, leading to the co-existence of multiple injuries. These findings suggest that clinically, when diagnosing and treating a certain type of injury, especially for cerebrovascular injuries, great vigilance should be paid to the occurrence of other related injuries, and comprehensive assessment and integrated treatment are necessary.

This study has certain limitations. The research subjects are only some neonates from specific regions, which leads to geographical limitations and may affect the general applicability of the results. The retrospective research method adopted is vulnerable to recall bias and selection bias. Moreover, due to conditional restrictions, some potential factors, such as gene polymorphisms and detailed information on intrauterine infections, have not been explored in depth.

Conclusion

This comprehensive analysis of 155 mother-infant pairs reveals critical sex-specific determinants of neonatal organ injury and establishes complex inter-organ injury relationships. The results indicated that birth weight and gestational age were significantly associated with the risk of organ injury. Regarding gender differences, we found that the risk of organ injury in male neonates was primarily significantly associated with gestational age and birth weight, while in female neonates, the risk was mainly associated with initial C-reactive protein levels. Notably, we identified profound co-occurrence patterns between cerebrovascular injuries, particularly the exceptionally strong correlation between cerebral infarction and hemorrhagic lesions. Our findings emphasize the importance of adopting gender-specific and individualized approaches in neonatal intensive care, while also considering maternal physiological conditions. These results provide specific evidence for improving neonatal care strategies and offer direction for future research, particularly in exploring the underlying mechanisms of gender differences and developing targeted prevention strategies.

Declarations:

Ethical Considerations

This study was approved by the Ethics Committee of Sichuan Provincial Maternal and Child Health Hospital. Due to the retrospective nature of the research, the requirement for obtaining informed consent from patients was waived. All patient data were anonymized to protect privacy.all methods were performed in accordance with the relevant guidelines and regulations.

Clinical trial number: not applicable.

Consent for publication: agree to publish

Conflicts of Interest: The authors declare no conflict of interest.

Data availability: All data generated or analysed during this study are included in this published article.

Informed consent waiver: The need for informed consent was waived by XYZ ethics committee.

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Authors' contributions: Zhihui Zou, Yuhang Li, and Dan Bai contributed equally to this work. Zhihui Zou designed the research, analyzed the data, and wrote the manuscript. Yuhang Li and Dan Bai performed the experiments and collected data. Desong Liu and Yanru Chen contributed to the analysis and interpretation of the results. Ting Hou and Jing Yang provided critical revisions to the manuscript. All authors read and approved the final manuscript.

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Supplementary materials

Table S1 Subgroup Analysis of Risk Factors for Neonatal Organ Injury by Sex

Variable	Sex	N	OR	CI_lower	CI_upper	P_value
Age (days)	Male	82	0.96	0.89	1.02	0.298
Age (days)	Female	73	1	0.93	1.06	0.993
Birth Weight (g)	Male	82	1	1	1	0.008
Birth Weight (g)	Female	73	1	1	1	0.197
Gestational Age (weeks)	Male	82	1.41	1.13	1.87	0.007
Gestational Age (weeks)	Female	73	1.08	0.92	1.29	0.373
1-min Apgar	Male	82	1.27	0.85	2.23	0.324
1-min Apgar	Female	73	1.3	0.89	2.4	0.272
5-min Apgar	Male	82	1.59	0.71	4.83	0.334
5-min Apgar	Female	73	1.13	0.58	2.94	0.739
10-min Apgar	Male	82	3.74	1	24.66	0.091
10-min Apgar	Female	73	1.14	0.4	3.99	0.821
Maternal Age (years)	Male	82	1.08	0.93	1.25	0.344
Maternal Age (years)	Female	73	0.91	0.81	1.01	0.101
Membrane Rupture (hours)	Male	82	1	0.99	1.01	0.922
Membrane Rupture (hours)	Female	73	1	0.99	1.01	0.848
Initial WBC (10^9/L)	Male	82	1	0.9	1.1	0.975

Initial WBC (10^9/L)	Female	73	1.01	0.9	1.12	0.914
Initial PLT (10^9/L)	Male	82	1	0.99	1.01	0.85
Initial PLT (10^9/L)	Female	73	1	1	1.01	0.719
Initial CRP (mg/L)	Male	82	0.99	0.89	1.07	0.788
Initial CRP (mg/L)	Female	73	1.14	1.01	1.31	0.045
Follow-up WBC (10^9/L)	Male	82	1.06	0.97	1.15	0.182
Follow-up WBC (10^9/L)	Female	73	0.95	0.86	1.03	0.292
Follow-up PLT (10^9/L)	Male	82	1	1	1.01	0.438
Follow-up PLT (10^9/L)	Female	73	1	1	1	0.702
Follow-up CRP (mg/L)	Male	82	0.98	0.85	1.07	0.657
Follow-up CRP (mg/L)	Female	73	1	0.9	1.08	0.916
PCT (ng/mL)	Male	82	5.76	0.02	1509.2	0.53
PCT (ng/mL)	Female	73	5.47	0.16	220.87	0.339
Invasive Ventilation (hours)	Male	82	1	0.99	1.01	0.809
Invasive Ventilation (hours)	Female	73	1	0.99	1	0.564
Non-invasive Ventilation (hours)	Male	82	1	1	1	0.036
Non-invasive Ventilation (hours)	Female	73	1	1	1	0.665
Antibiotics Duration (days)	Male	82	1.01	0.97	1.05	0.665
Antibiotics Duration (days)	Female	73	0.99	0.95	1.02	0.581
Weight Gain (g/day)	Male	82	1	1	1	0.55
Weight Gain (g/day)	Female	73	1	1	1	0.316
Time to Full Feeding (days)	Male	82	0.97	0.91	1.03	0.384
Time to Full Feeding (days)	Female	73	0.99	0.95	1.03	0.768