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ORIGINAL RESEARCH

Association of Birthweight Discordance with Adverse Birth Outcomes Among Live-Born Twins: A Multi-Center Study in China

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Background: Twin pregnancies, accounting for a rising proportion of births globally, present significant public health challenges in China. Birthweight discordance (BWD), a critical complication, remains understudied in its epidemiological context, particularly regarding its population-level associations with adverse neonatal outcomes.

Methods: This multi-center, retrospective cohort study leveraged data from 21 hospitals across 18 Chinese cities (2018–2020) to assess BWD and its epidemiological implications. Ordinal logistic regression with random effects was used to explore their association. BWD was defined as: [(*larger birthweight* − *smaller birthweight*) / *larger birthweight*] × 100% and categorized into four grades: I (≤15%), II (>15% to 20%), III (>20% to 25%), and IV (>25%).

Results: Among 6437 twin pairs, 73.6% were classified as Grade I (no BWD), while 10.7%, 7.1%, and 8.6% constituted Grades II, III, and IV discordance, respectively. Dose-response relationships emerged: each incremental BWD elevated risks of small vulnerable newborns (a*OR* = 1.83, 95% CI 1.76–1.90), small for gestational age (a*OR* = 1.23, 95% CI 1.18–1.29), low birthweight (LBW, a*OR* = 1.16, 95% CI 1.13–1.20), very LBW (a*OR* = 1.63, 95% CI 1.53–1.73) and extreme LBW (a*OR* = 1.82, 95% CI 1.61–2.05). Smaller twins exhibited disproportionately higher adverse outcome rates than larger twins. Sensitivity analyses confirmed robustness across specific subgroups.

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Conclusion: BWD exceeding 20% affects 15.7% of live-born twins in China, mirroring rates in high-income settings. BWD demonstrates strong dose-response relationships with adverse outcomes, validating its utility for twin health stratification. These findings call for integrating BWD assessment into prenatal surveillance and risk-adapted care to reduce neonatal morbidity/mortality, urging clinicians and policymakers to prioritize perinatal outcome equity.

Keywords: twins, birthweight discordance, perinatal epidemiology, adverse birth outcomes, public health, multi-center study

Introduction

Twin births represent a growing public health consideration, accounting for 2–4% of global deliveries with rates remaining stable in most regions.[1,2] In contrast, China has experienced a notable epidemiological shift: twin birth rates increased from 2.79% to 3.32% between 2011 and 2020, reflecting a 19% relative rise.[3] This upward trajectory underscores the urgency of investigating twin-specific health outcomes, particularly in light of their disproportionate contribution to perinatal morbidity and long-term healthcare burdens.

Birthweight (BW) serves as a critical proxy for fetal development and postnatal health risks.[4] In twin pregnancies, intertwin birthweight discordance (BWD)—defined as a percentage difference in BW between co-twins—emerges as a distinct epidemiological marker. While BW and BWD are correlated, they capture divergent biological pathways. BWD mechanisms remain poorly understood but may involve placental vascular anomalies, unequal cord insertion, or genetic/epigenetic disparities, all of which warrant population-level investigation.[5,6] Epidemiologically, BWD transcends individual clinical outcomes; it reflects systemic risks within maternal–fetal environments and may signal modifiable factors influencing twin health trajectories.

Existing evidence linking BWD to adverse outcomes—such as preterm birth, low birthweight, and neonatal mortality—remains inconsistent.[7–15] Heterogeneity in study designs, limited sample sizes, and geographic bias (with most data from Western populations) hinder generalizability.[16–18] Crucially, no large-scale epidemiological studies have quantified BWD-associated risks in China, where rising twin births coexist with unique sociodemographic and healthcare factors. For instance, regional disparities in prenatal care access, variations in maternal nutrition, and the widespread use of assisted reproductive technologies may differentially shape BWD patterns and outcomes. These gaps impede evidence-based policy-making and targeted interventions.

This multi-center epidemiological study leverages data from 21 hospitals across China to address three aims: (1) characterize the population-level distribution of BWD among live-born twins; (2) quantify associations between BWD severity and adverse birth outcomes (eg, respiratory distress, neonatal ICU admission); and (3) identify modifiable covariates (eg, gestational age, maternal comorbidities) that mediate these relationships. By integrating clinical and epidemiological frameworks, this work advances understanding of BWD as a preventable risk factor within China's evolving twin birth cohort. Findings will inform public health strategies to mitigate adverse outcomes, optimize resource allocation, and reduce disparities in twin neonatal care.

Methods

This multicenter cross-sectional study (Clinical Trial NCT05674214) adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Ethical approval was obtained from the Clinical Research and Application Committee of the Third Affiliated Hospital of Guangzhou Medical University, and informed consent was secured.

Study Design and Participants

This study was established by the collaborative study group for birthweight discordance in twin pregnancy (China), which was conducted between January 2021 and December 2022. In brief, we used a convenience cluster sampling strategy to recruit participants from 22 tertiary class-A hospitals with maternity and neonatal intensive care units (NICUs). We developed a standardized protocol to undertake a pilot multi-center study in Guangzhou city of Guangdong Province. We then followed the same protocol to undertake surveys in other study sites. As such, we generated a multi-center sample from five geographical regions of China, namely the Northern Region (Beijing, Cangzhou, Hohhot, Baotou, and Yanan), the Western Region (Chengdu, Guiyang, and Lanzhou), the Southern Region

(Guangzhou, Dongguan, Huizhou, Shaoguan, Zhongshan, and Shantou), the Central Region (Shaoyang, Xiaogan, and Xinxiang), and the Eastern Region (Xiamen). The detailed geographical distribution and specific characteristics of participating centers were delineated in eFigure 1 and eTable 1. The Third Affiliated Hospital of Guangzhou Medical University served as the research center, overseeing coordination, information integration, and data analysis.

Retrospectively, we examined 6821 twin pairs born at our study sites between January 2018 and December 2020. Exclusions encompassed twins from higher-order multiple pregnancies, cases involving twin to twin transfusion syndrome (TTTS), twin anemia polycythemia sequence (TAPS), monochorionic monoamniotic (MCMA) pregnancies, chromosomal abnormalities, and major congenital issues. Moreover, this investigation excluded data from the Xinxiang Central Hospital owing to its inapplicability (see more detail in eTable 1). Ultimately, 6437 pairs of live-born twins were included, as depicted in the participant enrollment flow diagram (Figure 1).

Data Collection

Study participants were identified through electronic medical record searches in each hospital based on twin pregnancy diagnosis and discharge year. Supervised by NICU directors in each site, data collection commenced in January 2021. Prior to collecting information on perinatal characteristics and adverse birth outcomes, all investigators underwent uniform training at each site. Consistent diagnostic criteria were applied across all NICUs throughout the study. Investigators inputted data into a customized standalone database using EpiData version 3.1 (EpiData Association). Each site performed double checks for accuracy and completeness, ensuring quality assurance, with all authors endorsing the process.

The research center designed and gained approval for a standardized questionnaire used at all study sites. Data concerning potential risk factors, maternal complications, distinctive twin traits, and other essential characteristics were recorded, including sex, zygosity of twin pregnancies, adverse pregnancy history, multipara status, advanced maternal age, ART use, mode of delivery, and maternal morbidity (gestational hypertension, gestational diabetes, placental disease, amniotic fluid disease, umbilical cord disease). We also obtained birth data encompassing gestational age (GA), BW, and Apgar scores.

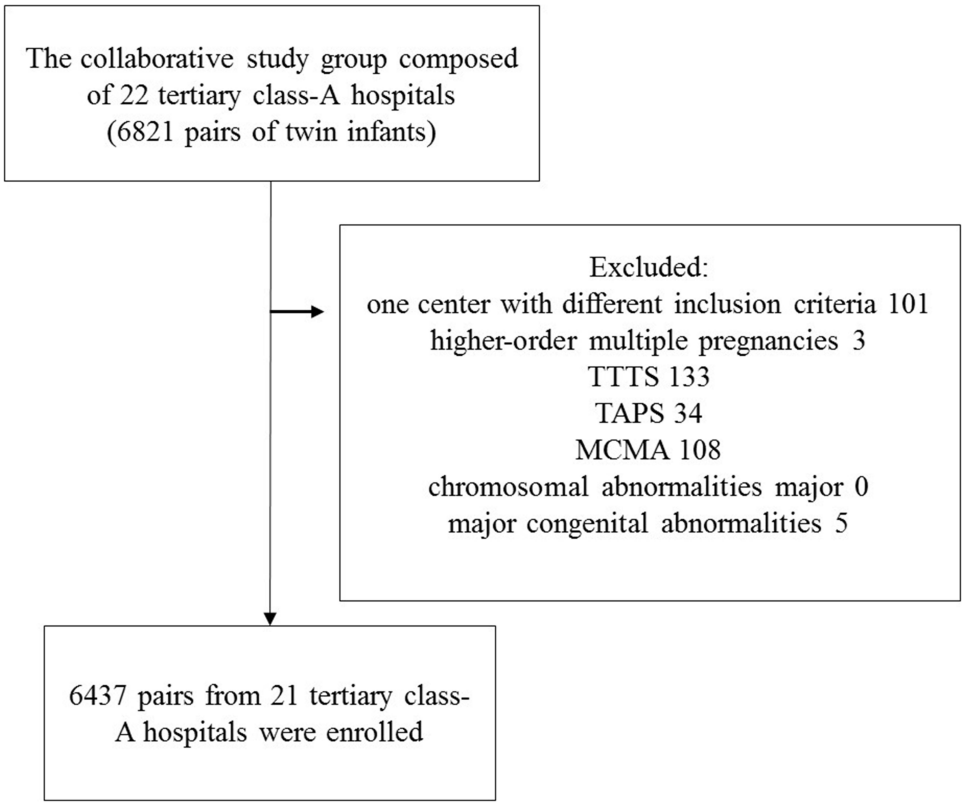

Figure 1 Participant flow diagram.

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Definitions

Birthweight discordance (BWD) was calculated as (larger BW - smaller BW)/larger BW× 100%. Given that extant evidence predominantly supports 15% or 20% as diagnostic thresholds for birthweight discordance, this study stratified BWD into four tiers: Grade I (≤15%), Grade II (>15% to 20%), Grade III (>20% to 25%), and Grade IV (>25%), to enhance analytical comprehensiveness. In this study, the following adverse birth outcomes including preterm birth (PTB), small for gestational age (SGA), low birthweight (LBW) and small vulnerable newborns (SVN) were used. Different levels of PTB and LBW were also defined using very PTB/LBW (VPTB and VLBW) and extremely PTB/LBW (EPTB and ELBW). Detailed descriptions of the above definitions can be found in eTable 2.

For each twin pair, adverse birth outcomes are defined as ordinal categorical variables except for preterm birth, which is a binary variable. They are encoded as follows: 0 signifies the absence of adverse birth outcomes, 1 indicates the presence of adverse birth outcomes for either of the twins, and 2 designates adverse birth outcomes for both twins.

Statistical Analysis

We describe the basic information of the live-born twins by calculating mean with standard deviation (SD) for continuous variables and percentages for categorical variables. The differences of twin pairs with different levels of BWD were compared using one-way analysis of variance for continuous variables and χ^2 tests for categorical variables.

We analyzed the associations of BWD (both continuous and categorical variables) with adverse birth outcomes by fitting traditional logistic regression with random effects for analyses of preterm birth and ordinal logistic regression with random effects for analyses of other adverse birth outcomes. We fitted crude models without adjustment with hospital as a random-effect variable, and fitted adjusted models for each outcome, adjusting for covariates including twin's sex, gestational age, zygosity of twin pregnancies, adverse pregnancy history, multipara status, advanced maternal age, ART use, mode of delivery, and maternal morbidity. Sensitivity analyses were performed to investigate the robustness of the results, by limiting the subject to the smaller and dichorionic diamniotic (DCDA) live-born twins.

Statistical analyses were conducted with the statistical software R, version 3.6.1 (R Core Team 2019). We present the results as odds ratios (*OR*s) with 95% confidence intervals (*CI*s). All tests were 2-sided and a $P < 0.05$ was considered statistically significant.

Results

We identified 6437 eligible infant pairs with a mean gestational age of 35.7 ± 2.3 weeks; 54.2% (n = 6976) were male, and 9.7% (n = 1251) were SGA. The mean BWD was 11.1 ± 9.3, and the prevalence of Grade I–IV BWD was 73.6% (n = 4735), 10.7% (n = 691), 7.1% (n=460) and 8.6% (n = 551), respectively. Table 1 summarized the study population's perinatal characteristics. Generally, there were significant differences among the mothers of twin pairs with different BWD in multipara status, ART use and dizygosity. The mothers of twin pairs with different BWD also showed significant different pregnancy complications in HDP, placental disease, amniotic fluid disease and umbilical cord disease. Twin pairs with different BWD showed significant group differences in their sex and GA.

As shown in Table 2, the prevalence of SVN, SGA, LBW, VLBW, ELBW, and low Apgar scores (≤7 at 1/5 minutes) was significantly higher in the smaller infants than in their larger co-twins (80.9% vs 68.0%, 17.2% vs 2.2%, 72.0% vs 45.3%, 8.7% vs 4.7%, 2.3% vs 1.2%, 6.3% vs 5.7%, 1.5% vs 1.4%, respectively). Generally, the prevalence of PTB, SVN, LBW, and lower Apgar score at 1 min were significantly higher among fetus with larger BWD than those with smaller BWD in both larger and smaller fetus. Additionally, there were significant differences of SGA, VLBW, and ELBW among smaller fetus with different levels of BWD. The eTable 3 summarized the prevalence of various adverse birth outcomes, which present in both live-born twins (67.7% for SVN, 2.2% for SGA, 62.9% for PTB, 7.6% for VPI, 1.5% for EPI, 45.3% for LBW, 4.7% for VLBW, 1.2% for ELBW, 2.7% for lower Apgar score at 1 min, 0.5% for lower Apgar score at 5 min, respectively). Besides, the prevalence of SVN, SGA, LBW, VLBW, ELBW, and lower Apgar score at 1 min in one of the twins were significantly higher among fetus with larger BWD than those with smaller BWD. However, the prevalence of those adverse outcomes in both twin were almost identical across different degrees of BWD.

Table 1 The Perinatal Characteristics of the Live-Born Twins and Their Mothers with Different Birthweight Discordance (in Four Categories)

	Birthweight Discordance				
	I-Degree (n = 4735)	**II-Degree (n = 691)**	**III-Degree (n = 460)**	**IV-Degree (n = 551)**	**Total (n = 6437)**
Maternal factors					
Advanced maternal age	1047 (22.1)	168 (24.3)	111 (24.1)	140 (25.4)	1466 (22.8)
Multipara status[α]	1942 (41.0)	253 (36.6)	152 (33.0)	190 (34.5)	2537 (39.4)
ART use[α]	2813 (59.4)	434 (62.8)	279 (60.7)	298 (54.1)	3824 (59.4)
Cesarean delivery	4311 (91.0)	643 (93.1)	425 (92.4)	506 (91.8)	5885 (91.4)
Dizygosity[α]	3734 (78.9)	559 (80.9)	366 (79.6)	408 (74.0)	5067 (78.7)
MCDA	1084 (22.9)	154 (22.3)	104 (22.6)	152 (27.6)	1494 (23.2)
Adverse pregnancy history	1981 (41.8)	270 (39.1)	199 (43.3)	220 (39.9)	2670 (41.5)
Pregnancy complications					
GDM	1041 (22.0)	149 (21.6)	100 (21.7)	116 (21.1)	1406 (21.8)
HDP[α]	693 (14.6)	113 (16.4)	87 (18.9)	144 (26.1)	1037 (16.1)
Placental disease[α]	369 (7.8)	55 (8.0)	43 (9.3)	65 (11.8)	532 (8.3)
Amniotic fluid disease[α]	275 (5.8)	40 (5.8)	26 (5.7)	78 (14.2)	419 (6.5)
Umbilical cord disease[α]	174 (3.7)	29 (4.2)	30 (6.5)	51 (9.3)	284 (4.4)
PROM	857 (18.1)	124 (17.9)	70 (15.2)	82 (14.9)	1133 (17.6)
Neonatal factors					
Sex[α]					
Male–male pairs	1746 (36.9)	220 (31.8)	170 (37.0)	221 (40.1)	2357 (36.6)
Female–male pairs	1641 (34.6)	274 (39.7)	170 (37.0)	177 (32.1)	2262 (35.1)
Female–female pairs	1348 (28.5)	197 (28.5)	120 (26.0)	153 (27.8)	1818 (28.3)
GA[α]	35.8 ± 2.3	35.7 ± 2.3	35.6 ± 2.2	35.3 ± 2.4	35.7 ± 2.3

Notes: I-degree: birthweight discordance ≤ 15%, II-degree: 15.01%-20%, III-degree: 20.01%-25%, and IV-degree: >25.01%. [α]The significant differences of twin pairs with different levels of BWD were identified using one-way analysis of variance for continuous variables and χ^2 tests for categorical variables.

Abbreviations: ART, assisted reproductive technology; GA, gestational age; GDM, gestational diabetes mellitus; HDP, hypertensive disorders of pregnancy; MCDA, monochorionic diamniotic; PROM, premature rupture of membranes.

Table 2 Prevalence of Adverse Birth Outcomes Among Live-Born Twins with Different Birthweight Discordance

Adverse Birth Outcomes	Birthweight Discordance				
	I-Degree (n = 4735)	**II-Degree (n = 691)**	**III-Degree (n = 460)**	**IV-Degree (n = 551)**	**Total (n = 6437)**
Preterm birth[α]	2916 (61.6)	425 (61.5)	305 (66.3)	400 (72.6)	4046 (62.9)
Very preterm infant	344 (7.3)	51 (7.4)	36 (7.8)	56 (10.2)	487 (7.6)
Extremely preterm infant	79 (1.7)	9 (1.3)	5 (1.1)	4 (0.7)	97 (1.5)
Small vulnerable newborns					
Larger fetus[α]	3205 (67.7)	444 (64.3)	320 (69.6)	411 (74.6)	4380 (68.0)
Smaller fetus[α]	3627 (76.6)	603 (87.3)	434 (94.3)	545 (98.9)	5209 (80.9)
Small for gestational age					
Larger fetus	112 (2.4)	8 (1.2)	10 (2.2)	14 (2.5)	144 (2.2)
Smaller fetus[α]	364 (7.7)	143 (20.7)	185 (40.2)	415 (75.3)	1107 (17.2)
Low birthweight					
Larger fetus[α]	2202 (46.5)	259 (37.5)	190 (41.3)	262 (47.5)	2913 (45.3)
Smaller fetus[α]	3086 (65.2)	581 (84.1)	424 (92.2)	545 (98.9)	4636 (72.0)

(*Continued*)

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Table 2 (Continued).

Adverse Birth Outcomes	Birthweight Discordance				
	I-Degree (n = 4735)	II-Degree (n = 691)	III-Degree (n = 460)	IV-Degree (n = 551)	Total (n = 6437)
Very low birthweight					
Larger fetus	227 (4.8)	30 (4.3)	17 (3.7)	28 (5.1)	302 (4.7)
Smaller fetus[α]	281 (5.9)	53 (7.7)	53 (11.5)	174 (31.6)	561 (8.7)
Extremely low birthweight					
Larger fetus	67 (1.4)	6 (0.9)	2 (0.4)	4 (0.7)	79 (1.2)
Smaller fetus[α]	78 (1.6)	14 (2.0)	8 (1.7)	45 (8.2)	145 (2.3)
APGAR Score 1-min ≤ 7					
Larger fetus[α]	242 (5.1)	48 (6.9)	35 (7.6)	44 (8.0)	369 (5.7)
Smaller fetus[α]	269 (5.7)	38 (5.5)	35 (7.6)	63 (11.4)	405 (6.3)
APGAR Score 5-min ≤ 7					
Larger fetus	67 (1.4)	6 (0.9)	6 (1.3)	9 (1.6)	88 (1.4)
Smaller fetus	65 (1.4)	10 (1.4)	10 (2.2)	13 (2.4)	98 (1.5)

Notes: I-degree: birthweight discordance ≤ 15%, II-degree: 15.01%-20%, III-degree: 20.01%-25%, and IV-degree: >25.01%. [α]The significant differences of twin pairs with different levels of BWD were identified using χ^2 tests for categorical variables.

We explore the adjusted associations of BWD or different degree of BWD with adverse birth outcomes (Tables 3 and 4). In the adjusted model, twin pairs with higher BWD showed higher risks of SVN, SGA and LBW among all twin pairs (*OR* = 1.826, 95% CI: 1.759–1.896 for SVN; *OR* = 1.230, 95% CI: 1.178–1.285 for SGA; *OR* = 1.161, 95% CI: 1.126–1.197 for LBW). Regarding different types of LBW, the associations were stronger for very LBW and extremely LBW (*OR* = 1.626, 95% CI: 1.530–1.727; *OR* = 1.817, 95% CI: 1.609–2.052, respectively). Twin pairs with higher degree of BWD also showed higher risks

Table 3 Associations Between Birthweight Discordance and Adverse Birth Outcomes Among Live-Born Twins in China Using Logistic/Ordinal Logistic Regression with Random Effects

Adverse Birth Outcomes	Crude Model		Adjusted Model	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Small vulnerable newborns[a]	1.84 (1.77, 1.91)	**<0.001**	1.83 (1.76, 1.90)	**<0.001**
Small for gestational age[a]	1.09 (1.05, 1.12)	**<0.001**	1.23 (1.18, 1.29)	**<0.001**
Preterm birth[b]	1.06 (1.03, 1.10)	**<0.001**	1.045 (1.01, 1.08)	**0.005**
Very preterm infant[b]	1.05 (0.99, 1.10)	0.058	1.064 (1.01, 1.12)	**0.015**
Extremely preterm infant[b]	0.85 (0.75, 0.97)	**0.016**	0.871 (0.75, 1.00)	0.061
Low birthweight[a]	1.11 (1.09, 1.14)	**<0.001**	1.161 (1.13, 1.20)	**<0.001**
Very low birthweight[a]	1.37 (1.32, 1.42)	**<0.001**	1.626 (1.53, 1.73)	**<0.001**
Extremely lowbirthweight[a]	1.37 (1.29, 1.46)	**<0.001**	1.817 (1.61, 2.05)	**<0.001**
APGAR Score				
1-min ≤ 7[a]	1.13 (1.09, 1.18)	**<0.001**	1.12 (1.07, 1.17)	**<0.001**
5-min ≤ 7[a]	1.07 (0.99, 1.16)	0.097	1.04 (0.96, 1.12)	0.397

Notes: [a]Ordinal logistic regression with a hospital-level random intercept was used for crude model. Ordinal logistic regression with a hospital-level random intercept was used for adjusted model adjusted for twin's sex, gestational age, zygosity, adverse pregnancy history, multipara status, advanced maternal age, ART use, mode of delivery, and maternal morbidity (gestational hypertension, gestational diabetes, placental disease, amniotic fluid disease, umbilical cord disease). [b]Logistic regression with a hospital-level random intercept was used for crude model. Logistic regression with a hospital-level random intercept was used for adjusted model adjusted for twin's sex, gestational age, zygosity, adverse pregnancy history, multipara status, advanced maternal age, ART use, mode of delivery, and maternal morbidity (gestational hypertension, gestational diabetes, placental disease, amniotic fluid disease, umbilical cord disease). Bold numerical text in the *P* value column denotes statistically significant results ($P < 0.05$).

Abbreviations: OR, odd ratio; CI, confidence interval; *P* value, under the null hypothesis (H_o), the probability of obtaining the observed sample results, or more extreme results, occurring.

Table 4 Adjusted Associations Between Birthweight Discordance (in Four Categories) and Adverse Birth Outcomes Among Live-Born Twins in China Using Logistic/Ordinal Logistic Regression with Random Effects

Adverse Birth Outcomes	Birthweight Discordance, OR (95% CI) with *P* value							
	≤15%	>15% to 20%		>20% to 25%		>25%		
Small vulnerable newborns[a]	**Reference**	1.47 (1.18, 1.83)	**0.001**	1.90 (1.45, 2.48)	**<0.001**	2.87 (2.15, 3.82)	**<0.001**
Small for gestational age[a]	**Reference**	3.20 (2.57, 3.98)	**<0.001**	7.88 (6.32, 9.82)	**<0.001**	23.07 (18.86, 28.21)	**<0.001**
Preterm birth[b]	**Reference**	0.96 (0.81, 1.14)	0.642	1.21 (0.98, 1.49)	0.077	1.53 (1.25, 1.87)	**<0.001**
Very preterm infant[b]	**Reference**	0.99 (0.73, 1.34)	0.947	1.05 (0.74, 1.51)	0.781	1.37 (1.02, 1.85)	**0.038**
Extremely preterm infant[b]	**Reference**	0.77 (0.39, 1.53)	0.461	0.65 (0.26, 1.59)	0.344	0.42 (0.16, 1.15)	0.091
Low birthweight[a]	**Reference**	1.32 (1.12, 1.56)	**0.001**	1.62 (1.33, 1.98)	**<0.001**	1.90 (1.56, 2.30)	**<0.001**
Very low birthweight[a]	**Reference**	1.77 (1.12, 2.80)	**0.015**	3.90 (2.47, 6.17)	**<0.001**	17.86 (12.31, 25.91)	**<0.001**
Extremely low birthweight[a]	**Reference**	1.79 (0.77, 4.15)	0.176	1.69 (0.57, 5.04)	0.344	20.95 (10.14, 43.29)	**<0.001**
APGAR Score							
1-min ≤ 7[a]	**Reference**	1.26 (0.93, 1.71)	0.137	1.54 (1.09, 2.17)	**0.013**	1.63 (1.22, 2.18)	**0.001**
5-min ≤ 7[a]	**Reference**	1.02 (0.57, 1.85)	0.944	1.19 (0.62, 2.26)	0.599	1.11 (0.65, 1.91)	0.698

Notes: [a]Ordinal logistic regression with a hospital-level random intercept was used for adjusted model adjusted for twin's sex, gestational age, monozygosity or dizygosity, bad obstetrics history, multipara status, advanced maternal age, ART use, mode of delivery, and maternal morbidity (gestational hypertension, gestational diabetes, placental disease, amniotic fluid disease, umbilical cord disease). [b]Logistic regression with a hospital-level random intercept was used for adjusted model adjusted for twin's sex, gestational age, monozygosity or dizygosity, bad obstetrics history, multipara status, advanced maternal age, assisted reproductive technology (ART) use, mode of delivery, and maternal morbidity (gestational hypertension, gestational diabetes, placental disease, amniotic fluid disease, umbilical cord disease). Bold numerical text in the *P* value column denotes statistically significant results ($P < 0.05$).

Abbreviations: OR, odd ratio; CI, confidence interval; *P* value, under the null hypothesis (H_o), the probability of obtaining the observed sample results, or more extreme results, occurring.

of the above adverse birth outcomes (Table 4). Twin pairs with higher BWD or higher degree of BWD showed higher risks of PTB (*OR* = 1.045, 95% CI: 1.013–1.078). Regarding different types of PTB, twin pairs with higher BWD or higher degree of BWD showed higher risks of very PTB, but there were no associations regarding BWD or different degree of BWD with extremely PTB. Twin pairs with higher BWD or higher degree of BWD also showed higher risks of APGAR 1-min score ≤ 7, but there were no associations regarding BWD or different degree of BWD with APGAR 5-min score.

Sensitivity analyses were conducted to verify the stability of the results by analyzing these outcomes among smaller and DCDA live-born twins (see eTables 4–7). As the results showed, the association remained consistent under various conditions.

Discussion

This multi-center epidemiological study elucidates the population-level burden of birthweight discordance (BWD) among live-born twins in China and its robust associations with adverse neonatal outcomes. Our findings reveal that increasing BWD severity significantly elevates the risks of low birthweight (LBW), small-for-gestational-age (SGA), and neonatal morbidity, while no associations were observed with extreme preterm birth (PTB) or 5-minute APGAR scores. These results underscore BWD as a critical epidemiological marker for twin health stratification, with implications for targeted perinatal care and resource allocation in rapidly evolving healthcare systems.

Epidemiological Burden and Regional Heterogeneity

We report a prevalence of 15.7% for moderate-to-severe BWD (grades III–IV) among live-born twins, aligning with rates in high-income countries (16.0–16.9%).[9,18] However, prior regional studies in China exhibited wide variability (8.0–22.7%),[19–21] likely due to inconsistent inclusion criteria (eg, contained twins with twin-to-twin transfusion syndrome [TTTS] or anemia-polycythemia sequence [TAPS]).[16,22] Whether it is TTTS or TAPS, both have specific pathological mechanism and even result in the death of one fetus in utero,[23,24] which are different from the BWD as defined in this article. By standardizing inclusion criteria across 21 centers, our study provides the first multi-regional representative estimates, addressing a critical gap in understanding BWD distribution in low- and middle-income settings. This heterogeneity highlights the need for harmonized diagnostic protocols to improve surveillance accuracy and comparability across regions.

BWD as a Predictor of Adverse Outcomes: Epidemiological Insights

Consistent with global evidence,[7,25–29] our ordinal regression models demonstrated dose-response relationships between BWD severity and LBW/SGA risks, even after adjusting for gestational age and maternal comorbidities. Notably, traditional neonatal indicators (eg, APGAR scores) showed limited sensitivity to BWD, whereas the novel Small Vulnerable Newborn (SVN) classification—integrating PTB, LBW, and SGA—emerged as a more holistic outcome measure.[30] This finding challenges current clinical paradigms that prioritize isolated metrics and advocates for SVN adoption in twin-specific risk stratification. Epidemiologically, SVN's broader scope aligns with the multifactorial nature of BWD-related morbidity, offering policymakers a unified framework to allocate neonatal intensive care resources.

Clinical and Public Health Implications

The strong association between BWD and LBW/SGA—observed even at mild discordance (grade II)—suggests that current thresholds for intervention (eg, ≥20–25% BWD) may be insufficient.[31] Early identification of BWD through routine ultrasound biometrics[32–34] could enable preemptive interventions, such as optimizing maternal nutrition or timing elective deliveries, to mitigate downstream healthcare burdens. Furthermore, regional disparities in prenatal care access —exacerbated by uneven distribution of assisted reproductive technologies—demand equity-focused policies. For instance, integrating BWD screening into China's tiered maternal care system could standardize risk assessment across urban and rural settings.

Methodological Strengths and Limitations

This study's power derives from its population-based design, encompassing diverse geographic and socioeconomic contexts to enhance generalizability. However, several limitations warrant caution. First, retrospective data collection risks residual confounding, despite rigorous standardization protocols. Secondly, we lacked ultrasound-based estimation of fetal weight, making it unclear when the significant BWD specifically occurred. Thirdly, despite multi-center sampling, over-representation of Southern China (particularly Guangdong) limits nationwide generalizability. Nevertheless, incorporating hospitals as random effects in mixed models partially mitigated this bias by accounting for cluster-level variations, thereby enhancing the robustness of our findings.

Future Directions

Prospective studies should explore BWD's etiological pathways, including placental vascular anomalies and epigenetic factors, to inform preventive strategies. Additionally, evaluating the cost-benefit of early BWD screening—coupled with interventions like antenatal corticosteroids or targeted neonatal resuscitation—could optimize clinical guidelines. Internationally, comparative studies between Chinese and Western cohorts may disentangle genetic, environmental, and healthcare system contributors to BWD disparities. Advances in fetal surgery and prenatal diagnostics present transformative opportunities for managing severe BWD.[35,36] For instance, high-resolution Doppler ultrasound can identify placental vascular anomalies as early as 16–20 weeks' gestation,[37] providing a window for preemptive interventions.

Conclusions

In China's context of rising twin births, BWD represents a modifiable risk factor with significant epidemiological and clinical ramifications. Our findings advocate for BWD's integration into national twin surveillance systems and underscore the urgency of interdisciplinary collaboration—obstetrics, neonatology, and public health—to reduce adverse outcomes. By prioritizing BWD in perinatal care frameworks, policymakers can advance equitable health outcomes for twins, aligning with global Sustainable Development Goals for neonatal survival.

Data Sharing Statement

Deidentified participant data will be made available upon reasonable request. Data requests may be submitted to the corresponding author at [cuiql_gysy@163.com] within 6 months to 5 years post-publication. Requestor must provide: methodologically sound proposal, signed data use agreement, institutional review board approval.

Transfer will occur via encrypted platform after proposal approval by the steering committee (response within 4 weeks).

Ethics Approval and Consent to Participate

The study was registered in the ClinicalTrials.gov (NCT05674214) and approved by the Clinical Research and Application Committee of the Third Affiliated Hospital of Guangzhou Medical University ([2020] No.097). Written informed consent was obtained from all participants' parent. All methods were performed in accordance with the ethical standards as laid down in the Declaration of Helsinki and its later amendments.

Consent for Publication

Written informed consent for publication was obtained.

Data Types

Baseline demographics and pregnancy characteristics, outcome variables (birthweight, gestational age, Apgar scores).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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