

Parenteral Nutrition, Microplastic Burden, and Bronchopulmonary Dysplasia Severity in Preterm Infants: A Prospective Observational Study

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Research Article

Keywords: microplastics, parenteral nutrition, bronchopulmonary dysplasia, preterm infants, dose-response relationship

Posted Date: October 22nd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10964310/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Microplastics (MPs) have been detected in human blood and various tissues, raising concerns about their potential health effects. Preterm infants receiving parenteral nutrition (PN) may be at risk of iatrogenic MP exposure through plastic infusion systems. However, whether PN-associated MP burden is associated with bronchopulmonary dysplasia (BPD) severity remains unknown.

Methods

This prospective observational study enrolled 29 preterm infants diagnosed with BPD at the Department of Neonatology, Guangdong Provincial Second People's Hospital, Jinan University, between June 2024 and December 2025. BPD severity was classified as mild ($n = 12$), moderate ($n = 9$), or severe ($n = 8$) according to the NICHD 2018/NRN 2019 criteria. Peripheral blood samples were collected on the day of PN discontinuation. MP particle count and mean size were measured using confocal micro-Raman spectroscopy. Comparisons among the three groups were performed using Kruskal–Wallis H test, Jonckheere–Terpstra trend test, and Spearman's rank correlation. Univariate ordinal logistic regression was used to identify factors associated with BPD severity.

Results

MP particle count and mean size increased progressively with BPD severity (both $P < 0.001$). PN duration was strongly correlated with MP particle count ($r = 0.862$, $P < 0.001$) and mean MP size ($r = 0.748$, $P < 0.001$). Univariate ordinal logistic regression showed that each 10-unit increase in MP particle count was associated with a 168% increase in the odds of more severe BPD (OR = 2.68, 95% CI: 1.74–4.13, $P < 0.001$); each 10- μm increase in mean MP size was associated with a 252% increase (OR = 3.52, 95% CI: 1.73–7.15, $P = 0.002$). PN duration was also significantly associated with BPD severity (OR = 1.32 per day, 95% CI: 1.14–1.53, $P < 0.001$). Sensitivity analysis confirmed that MP particle count remained independently associated with longer mechanical ventilation duration after adjusting for gestational age ($\beta = 1.85$, 95% CI: 0.50–3.20, $P = 0.008$).

Conclusions

PN duration is strongly correlated with circulating MP burden, and MP burden—particularly particle count and mean size—is independently associated with greater BPD severity in preterm infants. These findings suggest that MPs may serve as a previously unrecognized mediator linking prolonged PN to worse pulmonary outcomes, highlighting the need to monitor and reduce iatrogenic MP exposure in the NICU setting.

Study registration: ClinicalTrials.gov, NCT07326761.

Background

Bronchopulmonary dysplasia (BPD) is the most common chronic lung disease of prematurity and remains a leading cause of long-term respiratory and neurodevelopmental morbidity among very preterm infants [1, 2]. Despite substantial advances in neonatal intensive care—including antenatal corticosteroids, surfactant therapy, and lung-protective ventilation—the overall incidence of BPD has not declined appreciably over recent decades, largely attributable to the increased survival of extremely preterm infants [3]. The pathogenesis of BPD is multifactorial, involving oxidative stress, pulmonary inflammation, arrested alveolar development, and dysregulated angiogenesis [4, 5]. Among the various modifiable factors, nutritional support during the early postnatal period has received growing attention as a critical determinant of lung injury and repair [6].

Parenteral nutrition (PN) is essential for preterm infants who cannot tolerate adequate enteral feeding during the first days to weeks of life. However, accumulating evidence suggests that prolonged PN may paradoxically increase the risk of BPD. A recent prospective national cohort study from South Korea demonstrated that PN duration exceeding 28 days was associated with a significantly higher risk of BPD (OR 1.51, 95% CI 1.10–2.08) [7]. Similarly, a Chinese retrospective study found that preterm infants who developed BPD had lower early amino acid and lipid intakes, suggesting a complex relationship between PN composition and pulmonary outcomes [8]. Nevertheless, the mechanisms through which PN contributes to BPD severity remain incompletely understood, and the role of iatrogenic exposures associated with PN delivery has been largely overlooked.

In recent years, microplastics (MPs)—plastic particles less than 5 mm in diameter—have emerged as a ubiquitous environmental contaminant with potential health implications. MPs have now been detected in multiple human biological matrices, including blood, heart tissue, placenta, breast milk, feces, and sputum [9, 10]. Once in the circulation, MPs can interact with vascular endothelial cells, trigger oxidative stress and inflammatory responses, and potentially distribute to distant organs [11]. Experimental studies have demonstrated that MP exposure induces pulmonary inflammation, disrupts the alveolar–capillary barrier, promotes reactive oxygen species generation, and may contribute to pulmonary fibrosis [12, 13]. Importantly, the biological toxicity of MPs appears to be size-dependent, with smaller particles exhibiting greater cellular reactivity [14].

For preterm infants receiving PN, the infusion delivery system itself may constitute a continuous and iatrogenic source of MP exposure. The entire plastic pathway—comprising polyvinyl chloride (PVC) tubing, connectors, syringes, and PN solution bags—can release MPs during infusion, particularly when lipid emulsions are administered [15]. An *ex vivo* study specifically examining MP migration from neonatal PN circuits confirmed the release of MPs from infused solutions [16]. Furthermore, intravenous infusion has been identified as an unrecognized but significant route for internal MP exposure in hospitalized patients, with MPs detected in infusion products at an average abundance of 1.24 ± 1.44 items per unit, predominantly as fragmented polyethylene and polypropylene particles ranging from 15 to 100 μm in size [17]. Given that preterm infants often receive PN for days to weeks during a critical window of rapid lung development, the cumulative MP burden from prolonged PN may represent a novel, previously overlooked mechanism linking PN duration to BPD severity.

However, no study to date has directly quantified the relationship between PN duration, circulating MP burden, and BPD severity in preterm infants. While the association between prolonged PN and BPD is increasingly recognized, and while MPs have been detected in both human blood and PN delivery systems, the critical missing link—whether MP accumulation from PN independently contributes to the graded severity of BPD—remains unexplored.

To address this gap, we conducted a prospective observational study to compare MP burden (particle count and mean size) across mild, moderate, and severe BPD groups, to evaluate the correlation between PN duration and MP load, and to determine whether MP burden independently associates with BPD severity after accounting for relevant confounders. We hypothesized that prolonged PN duration would correlate with higher MP accumulation, and that greater MP burden would be independently associated with more severe BPD.

Methods

Study design and participants

This was a prospective, single-center observational cohort study conducted at the Department of Neonatology, Guangdong Provincial Second People's Hospital, Jinan University, Guangzhou, China, between June 1, 2024, and December 31, 2025. The study protocol was approved by the Institutional Ethics Committee of Guangdong Provincial Second People's Hospital and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians of all participating infants prior to enrollment.

Preterm infants who were diagnosed with bronchopulmonary dysplasia (BPD) were consecutively enrolled. BPD was diagnosed and graded according to the National Institute of Child Health and Human Development (NICHD) 2018 and Neonatal Research Network (NRN) 2019 criteria. For infants born at < 32 weeks of gestation, BPD was defined as the need for any respiratory support (supplemental oxygen, nasal cannula, continuous positive airway pressure, or mechanical ventilation) for at least 28 consecutive days. Severity was graded at 36 weeks postmenstrual age (PMA) based on the level of respiratory support as follows: Grade 0 (no supplemental oxygen, breathing room air); Grade 1 (mild) (nasal cannula $\leq$ 2 L/min); Grade 2 (moderate) (nasal cannula > 2 L/min, nasal continuous positive airway pressure [nCPAP], or non-invasive positive pressure ventilation [NIPPV]); and Grade 3 (severe) (invasive mechanical ventilation [intubation]). For infants born at $\geq$ 32 weeks of gestation, BPD was defined as the need for supplemental oxygen for at least 28 consecutive days, with severity graded at 56 days of life using the same respiratory support-based criteria.

Exclusion criteria were: (1) major congenital anomalies or genetic syndromes; (2) congenital heart disease requiring surgical intervention; (3) severe perinatal asphyxia (Apgar score < 3 at 5 minutes); and (4) Death within 28 days after birth. A total of 29 infants were ultimately enrolled and classified into three groups: mild (n = 12), moderate (n = 9), and severe (n = 8).

Data collection

Maternal and neonatal demographic and clinical data were prospectively recorded, including gestational age, birth weight, mode of delivery, antenatal corticosteroid use, sex, and duration of invasive mechanical ventilation. The primary exposure variable was duration of parenteral nutrition (PN), defined as the total number of days on which the infant received intravenous nutrition via a central or peripheral venous catheter.

Blood sample collection and microplastic detection

Peripheral venous blood samples (2–3 mL) were prospectively collected from each infant on the day of parenteral nutrition discontinuation, defined as the last day on which the infant received any intravenous nutrition (amino acids, lipids, or dextrose). This time point was chosen to capture the cumulative MP burden at the end of the PN exposure period, prior to the final BPD severity assessment, thereby establishing a clear temporal sequence between MP measurement and outcome determination. Samples were collected using metal-free, glass syringes to minimize external microplastic (MP) contamination and were immediately transferred into pre-cleaned glass vials containing sodium citrate as anticoagulant. All samples were immediately frozen and stored at -80°C until laboratory processing.

Samples were transferred to glass bottles, digested, and filtered through a membrane. The resulting filters were analyzed using a confocal micro-Raman spectrometer. All test tubes, beakers, and pipettes used during processing were made of glass and had not come into contact with plastic products. Confocal micro-Raman spectroscopy identifies particles through Raman scattering and, when combined with confocal microscopy, supports point-by-point mapping of microplastic composition and distribution.

Outcome definition

The primary outcome of this study was BPD severity, classified as mild, moderate, or severe according to the NICHD 2018/NRN 2019 criteria (detailed in Section 2.1). The classification was performed prospectively by two attending neonatologists who were blinded to the MP measurement results.

Statistical analysis

All statistical analyses were performed using R software version 4.3.2 and SPSS version 26.0. Continuous variables were assessed for normality using the Shapiro–Wilk test; non-normally distributed data were presented as mean $\pm$ standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Comparisons among the three BPD severity groups were performed using the Kruskal–Wallis H test for continuous variables and the Pearson chi-square test or Fisher’s exact test for categorical variables. The Jonckheere–Terpstra test was used to assess linear trends across the ordered groups for microplastic parameters and PN duration.

Spearman's rank correlation coefficients were calculated to evaluate the associations between PN duration, MP burden (particle count and mean size), and duration of invasive mechanical ventilation. To identify factors independently associated with BPD severity, we performed univariate ordinal logistic regression with BPD severity as the dependent variable (mild = 1, moderate = 2, severe = 3). Separate models were constructed for each exposure variable (PN duration, MP particle count, and mean MP size) to avoid multicollinearity, given the strong correlations between these variables. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Additionally, a sensitivity analysis was conducted using multiple linear regression with duration of invasive mechanical ventilation as the dependent variable to further validate the independent effect of MP burden. A two-sided $p < 0.05$ was considered statistically significant for all analyses.

Results

Microplastic types

In the blood samples of all infants, a total of three types of microplastic particles were detected, namely polyethylene (PE), polypropylene (PP), and polyvinyl siloxane (PVS) (Fig. 1). These are all common microplastic types found in infusion tubing. PE was detectable in all blood samples across all infants. PP was detected in one infant in the severe BPD group, and PVS was detected in two infants in the severe group; no PP or PVS particles were detected in the remaining infants.

Baseline characteristics

A total of 29 preterm infants diagnosed with BPD were enrolled in this study, including 12 with mild BPD, 9 with moderate BPD, and 8 with severe BPD. The baseline characteristics of the three groups are summarized in Table 1.

Gestational age and birth weight decreased progressively with increasing BPD severity (both $P < 0.001$). The mean gestational age was 30.02 ± 1.00 weeks in the mild group, 27.84 ± 1.00 weeks in the moderate group, and 26.35 ± 0.83 weeks in the severe group. Similarly, mean birth weight was 1216.67 ± 197.84 g in the mild group, 945.56 ± 110.40 g in the moderate group, and 710.00 ± 70.71 g in the severe group.

There were no significant differences among the three groups in mode of delivery, antenatal corticosteroid use, or sex distribution (all $P > 0.05$). However, duration of invasive mechanical ventilation increased significantly with BPD severity ($P < 0.001$), with mean durations of 4.17 ± 1.95 days in the mild group, 12.78 ± 4.35 days in the moderate group, and 21.75 ± 3.84 days in the severe group.

Table 1
Baseline Characteristics of Preterm Infants Across BPD Severity Groups

Variable	Mild (n = 12)	Moderate (n = 9)	Severe (n = 8)	Statistical value	P value
Gestational age (weeks)	30.02 ± 1.00	27.84 ± 1.00	26.35 ± 0.83	H = 22.52	< 0.001
Birth weight (g)	1216.67 ± 197.84	945.56 ± 110.40	710.00 ± 70.71	H = 23.81	< 0.001
Cesarean section [n (%)]	8 (66.7)	6 (66.7)	6 (75.0)	$\chi^2 = 0.19$	0.908
Antenatal corticosteroids [n (%)]	10 (83.3)	7 (77.8)	7 (87.5)	$\chi^2 = 0.31$	0.854
Male [n (%)]	9 (75.0)	7 (77.8)	6 (75.0)	$\chi^2 = 0.03$	0.987
Invasive mechanical ventilation (days)	4.17 ± 1.95	12.78 ± 4.35	21.75 ± 3.84	H = 24.81	< 0.001
Note: Continuous variables are presented as mean ± SD and compared using the Kruskal–Wallis H test. Categorical variables are presented as n (%) and compared using the Pearson χ^2 test.					

Parenteral nutrition duration and microplastic burden across BPD severity groups

Table 2 presents the comparison of PN duration and MP burden among the three BPD severity groups. PN duration increased progressively from the mild to the severe BPD group: 16.08 ± 4.23 days in the mild group, 25.33 ± 4.90 days in the moderate group, and 37.00 ± 5.93 days in the severe group (P < 0.001). Similarly, all three MP metrics showed significant stepwise increases across the three groups. MP particle count was 13.08 ± 4.64 in the mild group, 50.67 ± 13.17 in the moderate group, and 61.50 ± 11.41 in the severe group (P < 0.001). Mean MP size was 27.12 ± 7.73 µm in the mild group, 40.51 ± 4.40 µm in the moderate group, and 45.11 ± 5.88 µm in the severe group (P < 0.001). The number of particles > 60 µm also increased from 0.25 ± 0.45 in the mild group to 2.11 ± 1.27 in the moderate group and 5.50 ± 1.93 in the severe group (P < 0.001).

The Jonckheere–Terpstra trend test confirmed a significant dose-response trend for all MP parameters and PN duration across the ordered BPD severity groups (all P < 0.001). Figure 2A and 2B visually depict the distribution and increasing trends of MP particle count and mean MP size across the three groups.

Table 2
Parenteral Nutrition Duration and Microplastic Burden Across BPD Severity Groups

Variable	Mild (n = 12)	Moderate (n = 9)	Severe (n = 8)	H value	P value
PN duration (days)	16.08 ± 4.23	25.33 ± 4.90	37.00 ± 5.93	24.03	< 0.001
MP particle count (n)	13.08 ± 4.64	50.67 ± 13.17	61.50 ± 11.41	23.74	< 0.001
Mean MP size (µm)	27.12 ± 7.73	40.51 ± 4.40	45.11 ± 5.88	21.56	< 0.001
Particles > 60 µm (n)	0.25 ± 0.45	2.11 ± 1.27	5.50 ± 1.93	22.18	< 0.001
Note: Data are presented as mean ± SD. Comparisons among groups were performed using the Kruskal–Wallis H test. The Jonckheere–Terpstra trend test confirmed significant dose-response trends for all parameters across BPD severity groups (all $P < 0.001$).					

Correlations among PN duration, microplastic burden, and mechanical ventilation

Spearman’s rank correlation analysis was performed to evaluate the associations between PN duration, MP burden, and duration of invasive mechanical ventilation. The complete correlation matrix is presented in Table 3. PN duration was strongly positively correlated with MP particle count ($r = 0.862$, $P < 0.001$) and mean MP size ($r = 0.748$, $P < 0.001$), as visually demonstrated in Fig. 3 with the fitted regression line and 95% confidence interval. MP particle count was also strongly correlated with duration of invasive mechanical ventilation ($r = 0.855$, $P < 0.001$). Additionally, MP particle count showed a strong positive correlation with mean MP size ($r = 0.758$, $P < 0.001$).

Gestational age was negatively correlated with PN duration ($r = -0.853$, $P < 0.001$), MP particle count ($r = -0.782$, $P < 0.001$), mean MP size ($r = -0.743$, $P < 0.001$), and invasive mechanical ventilation duration ($r = -0.847$, $P < 0.001$), indicating that lower gestational age was associated with longer PN duration, higher MP burden, and longer ventilation requirements.

Table 3
Spearman’s Rank Correlation Coefficients Among Key Clinical Variables and Microplastic Burden

Variable	PN duration	Invasive MV duration	MP particle count	Mean MP size
Gestational age	-0.853	-0.847	-0.782	-0.743
PN duration	—	0.824	0.862	0.748
Invasive MV duration	—	—	0.855	0.751
MP particle count	—	—	—	0.758
Note: Values are Spearman’s rho (r). All correlation coefficients are statistically significant ($P < 0.001$).				

Regression analyses for factors associated with BPD severity and sensitivity analysis

Univariate ordinal logistic regression was performed to identify factors associated with BPD severity. As presented in Table 4A and visualized in Fig. 4, each of the three exposure variables was significantly associated with increased odds of more severe BPD:

PN duration: each 1-day increase was associated with a 32% increase in the odds of more severe BPD (OR = 1.32, 95% CI: 1.14–1.53, P < 0.001).

MP particle count: each 10-unit increase was associated with a 168% increase in the odds of more severe BPD (OR = 2.68, 95% CI: 1.74–4.13, P < 0.001).

Mean MP size: each 10-μm increase was associated with a 252% increase in the odds of more severe BPD (OR = 3.52, 95% CI: 1.73–7.15, P = 0.002).

The forest plot (Fig. 4) shows that all three factors had ORs significantly greater than 1, with mean MP size demonstrating the strongest effect on BPD severity progression.

Table 4
A. Univariate Ordinal Logistic Regression for BPD Severity

Exposure variable	OR (95% CI)	P value
PN duration (per 1-day increase)	1.32 (1.14–1.53)	< 0.001
MP particle count (per 10-unit increase)	2.68 (1.74–4.13)	< 0.001
Mean MP size (per 10-μm increase)	3.52 (1.73–7.15)	0.002

To further validate the independent effect of MP burden on pulmonary morbidity, we performed a sensitivity analysis using multiple linear regression with duration of invasive mechanical ventilation as the dependent variable. As shown in Table 4B, after adjusting for gestational age:

MP particle count remained independently associated with longer duration of mechanical ventilation (β = 1.85 per 10-unit increase, 95% CI: 0.50–3.20, P = 0.008), indicating that each 10-unit increase in MP particles was associated with an additional 1.85 days of mechanical ventilation.

Gestational age was independently associated with shorter ventilation duration (β = -2.10 per 1-week increase, 95% CI: -2.80 to -1.40, P < 0.001), indicating that each additional week of gestational age reduced ventilation duration by approximately 2.10 days.

The model showed good fit (adjusted R² = 0.786, F = 52.64, P < 0.001). Variance inflation factor (VIF) values were < 2.0, indicating no significant multicollinearity.

Table 4

B. Sensitivity Analysis: Multiple Linear Regression with Invasive MV Duration as Dependent Variable

Independent variable	Unstandardized β	95% CI	P value
MP particle count (per 10-unit increase)	1.85	0.50–3.20	0.008
Gestational age (per 1-week increase)	-2.1	-2.80 – -1.40	< 0.001
Note: Model adjusted $R^2 = 0.786$, $F = 52.64$, $P < 0.001$. VIF < 2.0, indicating no significant multicollinearity.			

Discussion

In this prospective cohort study of 29 preterm infants with BPD, we observed three key findings: (1) MP burden—both particle count and mean size—increased progressively with BPD severity; (2) PN duration was strongly correlated with MP accumulation in the blood; and (3) PN duration, MP particle count, and mean MP size were each independently associated with greater BPD severity in univariate ordinal logistic regression analyses. To our knowledge, this is the first study to directly quantify the dose-response relationship between PN-associated MP exposure and BPD severity in preterm infants, providing novel evidence that MPs may serve as a previously unrecognized mediator linking prolonged PN to worse pulmonary outcomes.

The biological plausibility of our findings is supported by accumulating experimental evidence demonstrating the pulmonary toxicity of MPs. Microplastics can induce oxidative stress and inflammation in lung tissue through multiple pathways. Cao et al. demonstrated that chronic exposure to polystyrene microplastics (PS-MPs) triggers lung injury via targeting toll-like receptor 2 (TLR2) and activating the NF- κ B signaling pathway, and that inhibition of NF- κ B signaling relieves inflammation, oxidative stress, and apoptosis [18]. Additionally, PS-MPs have been shown to activate the NLRP3 inflammasome through endoplasmic reticulum stress, leading to pulmonary inflammation characterized by inflammatory cell infiltration and ultrastructural abnormalities [19]. More specifically, Zhang et al. demonstrated that PS-MPs induce pulmonary fibrosis by promoting alveolar epithelial cell ferroptosis through the cGAS/STING signaling pathway [13]. Traversa et al. showed that polyethylene micro/nanoplastics exposure induces epithelial–mesenchymal transition (EMT) in human bronchial and alveolar epithelial cells, a process implicated in aberrant tissue remodeling and fibrosis [20]. Furthermore, Lee et al. found that intravenous administration of environmentally relevant MPs in mice reduced key regulatory cytokines such as TGF- β and IL-10—which play critical roles in pulmonary regeneration and fibrosis—suggesting that MP exposure disrupts pulmonary repair and inflammatory resolution [21]. A recent comprehensive review further consolidates these findings, outlining how different polymer types, sizes, and aging states affect lung cells through inflammation, oxidative stress, ferroptosis, epithelial–mesenchymal transition, and epigenetic changes [22]. Given that BPD is characterized by arrested alveolar development and dysregulated lung repair, it is biologically plausible that MPs—by inducing oxidative stress, activating pro-inflammatory pathways, and impairing tissue

repair mechanisms—could exacerbate the underlying pathophysiological processes that drive BPD severity.

Importantly, our finding that PN duration correlates strongly with MP burden ($r = 0.862$, $P < 0.001$) provides compelling evidence that the PN delivery system is a major iatrogenic source of MP exposure in preterm infants. This is consistent with recent experimental evidence. Importantly, our finding that PN duration correlates strongly with MP burden ($r = 0.862$, $P < 0.001$) provides compelling evidence that the PN delivery system is a major iatrogenic source of MP exposure in preterm infants. This is consistent with recent experimental evidence. Our group has previously reported, in a prospective cohort study of 12 neonates, that MP abundance in blood was significantly higher in infants receiving long-term PN (> 14 days) compared to those receiving short-term PN or no PN exposure, with polyethylene (PE) accounting for 95.65% of all detected particles [23]. Vercauteren et al. demonstrated in an ex vivo study that MPs migrate from infused neonatal PN circuits [16]. Furthermore, quantitative analysis by Zheng et al. revealed that brand-new disposable PVC infusion tubes carry an average of 931.4 PVC-MP particles, and that infusion tubes continue to release MPs with time and temperature increases [24]. Given that preterm infants often receive PN for weeks, the cumulative MP exposure from the PN circuit may be substantial. The strong correlation observed in our study—between PN duration and blood MP levels—provides in vivo human evidence that corroborates these experimental findings, supporting the notion that prolonged PN exposure drives MP accumulation.

Our study also revealed that mean MP size was the strongest predictor of BPD severity among the three exposure variables (OR = 3.52 per 10- μ m increase, 95% CI: 1.73–7.15, $P = 0.002$). This size-dependent effect is consistent with the well-established toxicological principle that particle size critically influences biological reactivity. Smaller particles generally exhibit greater cellular uptake and inflammatory potential due to their larger surface-to-volume ratio, while larger particles may cause mechanical obstruction or chronic foreign-body responses. The presence of $> 60 \mu\text{m}$ particles—which we found increased dramatically from the mild to the severe BPD group (0.25 ± 0.45 to 5.50 ± 1.93)—raises the possibility that larger MPs may physically embolize pulmonary microvessels or induce sustained granulomatous inflammation, contributing to the pulmonary vascular remodeling and alveolar simplification characteristic of severe BPD. This size-dependent toxicity gradient adds further biological credibility to the dose-response relationship we observed.

Several previous studies have investigated the relationship between PN and BPD. Kim et al., in a prospective national cohort study of 2,490 very-low-birth-weight infants in South Korea, demonstrated that PN duration exceeding 28 days was associated with a significantly higher risk of BPD (OR 1.51, 95% CI: 1.10–2.08) [7]. Xu et al. found that preterm infants who developed BPD had lower early amino acid and lipid intakes [8]. However, these studies did not measure MPs, and the mechanisms linking PN to BPD remained speculative. Our study extends this line of inquiry by identifying MPs as a measurable, biologically plausible mediator that may explain, at least in part, the observed association between prolonged PN and worse pulmonary outcomes. While the OR for PN duration in our study (1.32 per day)

appears modest, it reflects the incremental risk per additional day of exposure; the cumulative effect over weeks is clinically meaningful.

From a clinical perspective, our findings have several implications. First, MP burden measured at PN discontinuation may serve as an early biomarker for identifying infants at heightened risk of severe BPD, potentially allowing for targeted preventive strategies. Second, our results highlight the need to minimize MP exposure from PN delivery systems. Potential strategies include reducing PN duration when clinically feasible, using in-line filtration to remove MPs from infusates, and transitioning to non-PVC infusion materials. The use of non-PVC infusion sets has been advocated to reduce patient exposure to phthalate plasticizers; our data suggest that MP exposure provides an additional rationale for such replacements. Third, future studies should investigate whether antioxidant or anti-inflammatory interventions could mitigate MP-induced lung injury in this vulnerable population.

Several limitations of this study should be acknowledged. First, this was a single-center study with a relatively small sample size ($n = 29$), which limits the generalizability of our findings and precludes more complex multivariable modeling. Second, while we measured MP particle count and size, we did not characterize the polymer composition (e.g., polyethylene, polypropylene, polyvinyl chloride) of the MPs detected, which may have different toxicological profiles. Third, we collected blood samples at a single time point (PN discontinuation); serial measurements throughout the PN course would have provided stronger evidence for the accumulation trajectory of MPs. Fourth, we did not measure inflammatory biomarkers (e.g., IL-6, TNF- α , IL-10) in our cohort, which precludes direct exploration of the mechanistic pathway between MP exposure and lung injury. Fifth, although our study established a temporal sequence—MP measurement preceded final BPD severity assessment—the observational design cannot establish causality. Finally, the NICHD 2018/NRN 2019 BPD grading criteria we used, while more refined than previous versions, may not fully capture the heterogeneity of BPD pathophysiology.

Conclusions

In this prospective cohort study of 29 preterm infants with BPD, we demonstrated that PN duration is strongly correlated with circulating MP burden, and that MP burden—particularly particle count and mean size—is independently associated with greater BPD severity. To our knowledge, this is the first study to quantify the dose-response relationship between PN-associated MP exposure and BPD severity in preterm infants, suggesting that MPs may serve as a previously unrecognized mediator linking prolonged PN to worse pulmonary outcomes.

From a clinical perspective, MP burden measured at PN discontinuation may hold potential as an early biomarker for identifying infants at heightened risk of severe BPD. More importantly, our findings highlight the need to minimize iatrogenic MP exposure from PN delivery systems—through strategies such as reducing PN duration when clinically feasible, using in-line filtration, and transitioning to non-PVC infusion materials. In conclusion, this study provides the first human evidence that PN-associated MP

exposure is independently associated with BPD severity in preterm infants, underscoring the importance of monitoring and reducing MP exposure in the NICU setting.

Abbreviations

BPD
bronchopulmonary dysplasia
CI
confidence interval
MP
microplastic
NICHD
National Institute of Child Health and Human Development
NICU
neonatal intensive care unit
NIPPV
non-invasive positive-pressure ventilation
nCPAP
nasal continuous positive airway pressure
OR
odds ratio
PE
polyethylene
PMA
postmenstrual age
PN
parenteral nutrition
PP
polypropylene
PVC
polyvinyl chloride
PVS
polyvinyl siloxane
SD
standard deviation
VIF
variance inflation factor.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Ethics Committee of Guangdong Provincial Second People's Hospital. Written informed consent was obtained from the parents or legal guardians of all participating infants prior to enrollment.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding

This work was supported by the Guangdong Provincial Medical Science and Technology Research Fund Project (Grant No. B2026308), the Wu Jieping Medical Foundation (Grant No. 320.6750.2025-23-9), and the 2025 Guangzhou Basic Research Plan, jointly funded by the city and the school (Grant No. 2025A03J4438). The funders had no role in study design, data collection, analysis, interpretation, or manuscript writing.

Authors' contributions

Debo Xu: Data curation, Software, Supervision, Writing – original draft, Writing – review & editing. Zhenyu Liang: Data curation, Software, Supervision, Writing – original draft, Writing – review & editing. Lingling Chen: Data curation, Writing – review & editing. Lin Li: Data curation, Validation, Writing – original draft. Huiyi Li: Investigation, Resources, Writing – original draft. Qiaohuan Yang: Data curation, Methodology, Supervision, Validation, Writing – review & editing, Writing – original draft. Qiong Meng and Wei Zhou: Data curation, Methodology, Supervision, Writing – review & editing, Writing – original draft. All authors have read and approved the final manuscript.

Acknowledgements

We sincerely thank all the infants and their families for their participation in this study. We also express our gratitude to the nursing staff of the Department of Neonatology, Guangdong Provincial Second People's Hospital, for their assistance in sample collection and clinical data recording. We are grateful to the laboratory technicians for their support in microplastic analysis.

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Figures

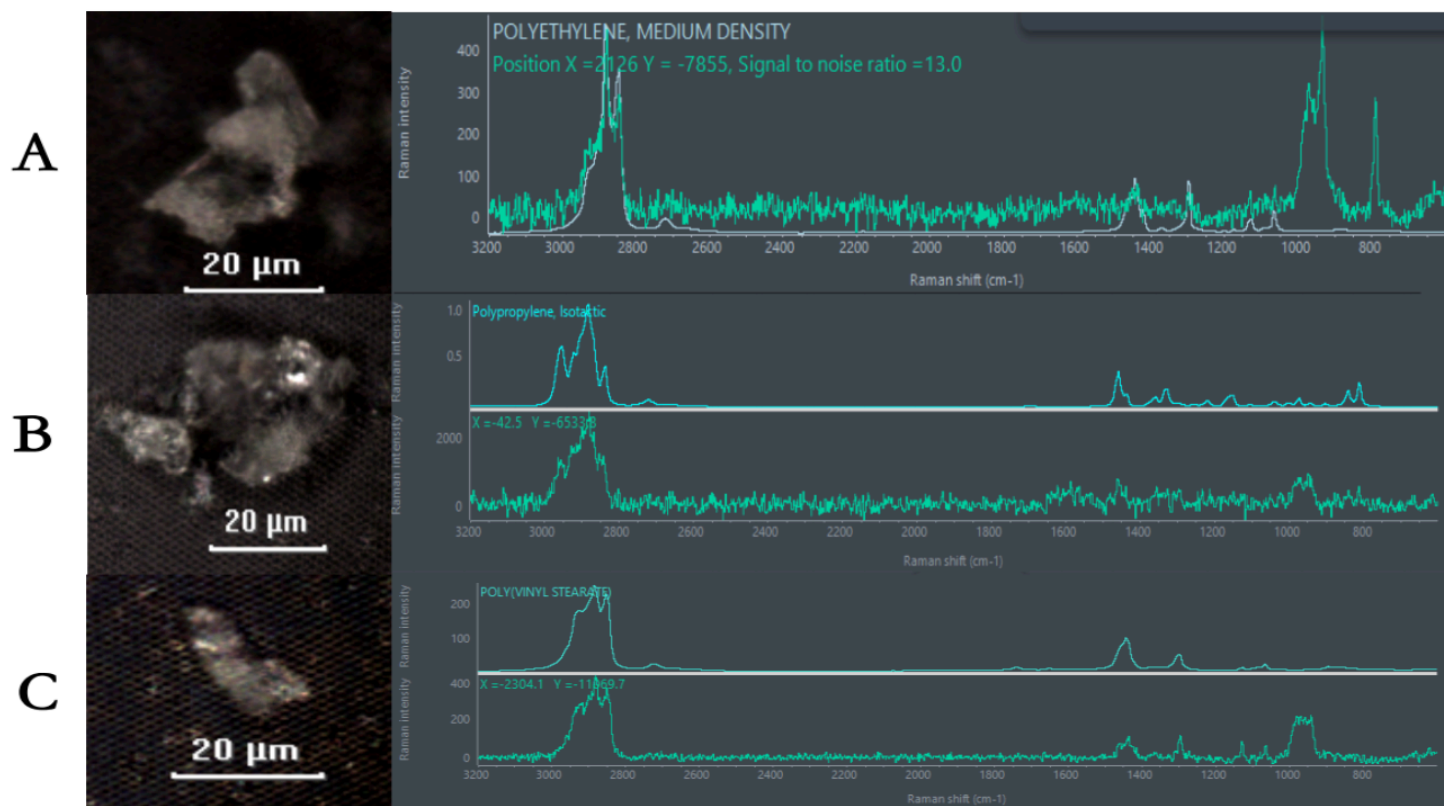


Figure 1

Microplastics detected in neonatal blood samples. Representative microscopic images and corresponding Raman spectra of particles detected in neonatal blood samples: (A) polyethylene (PE), (B) polypropylene (PP), and (C) polyvinyl siloxane (PVS).

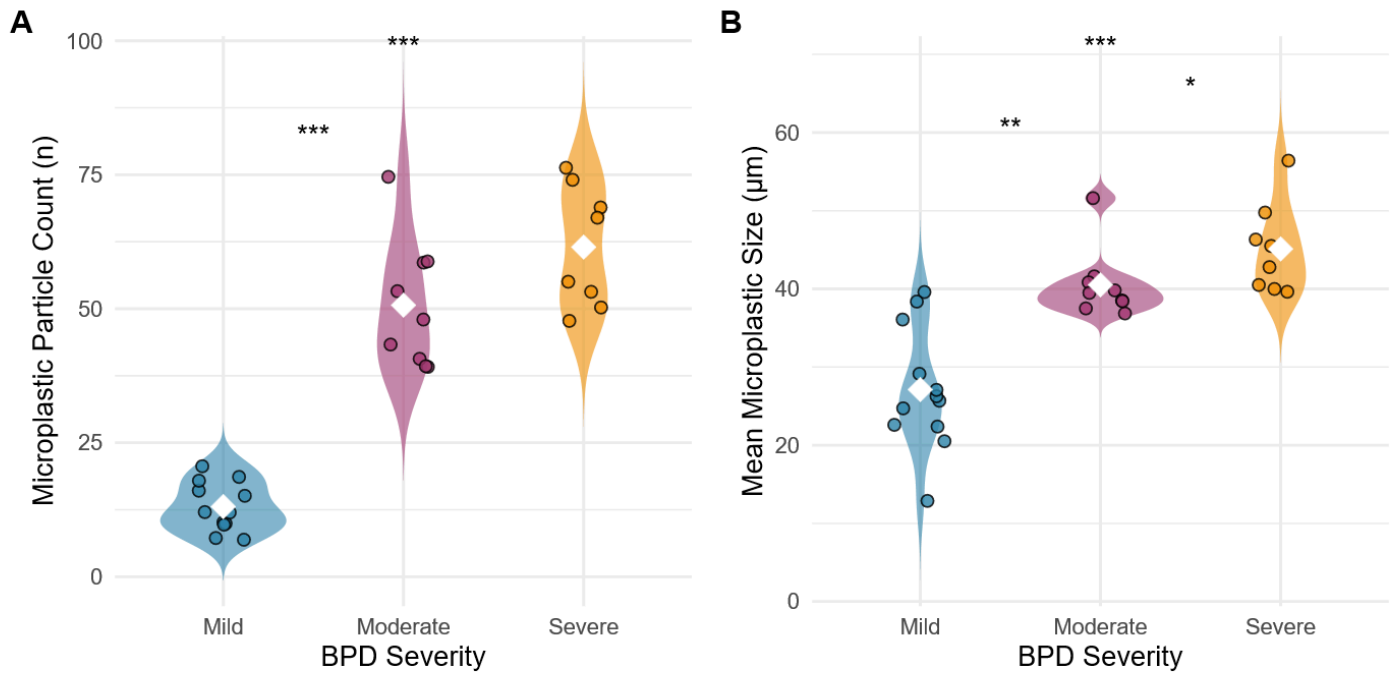


Figure 2

Microplastic burden across BPD severity groups. Violin plots show the distribution of (A) microplastic particle counts and (B) mean microplastic particle sizes among mild (n = 12), moderate (n = 9), and severe (n = 8) BPD groups. Violin width represents data density; jittered dots represent individual observations; white diamonds indicate group means. Significance levels were determined using Wilcoxon rank-sum tests: **P < 0.01, ***P < 0.001; NS, not significant. The Jonckheere-Terpstra trend test confirmed significant trends for both parameters across ordered BPD severity groups (both P < 0.001).

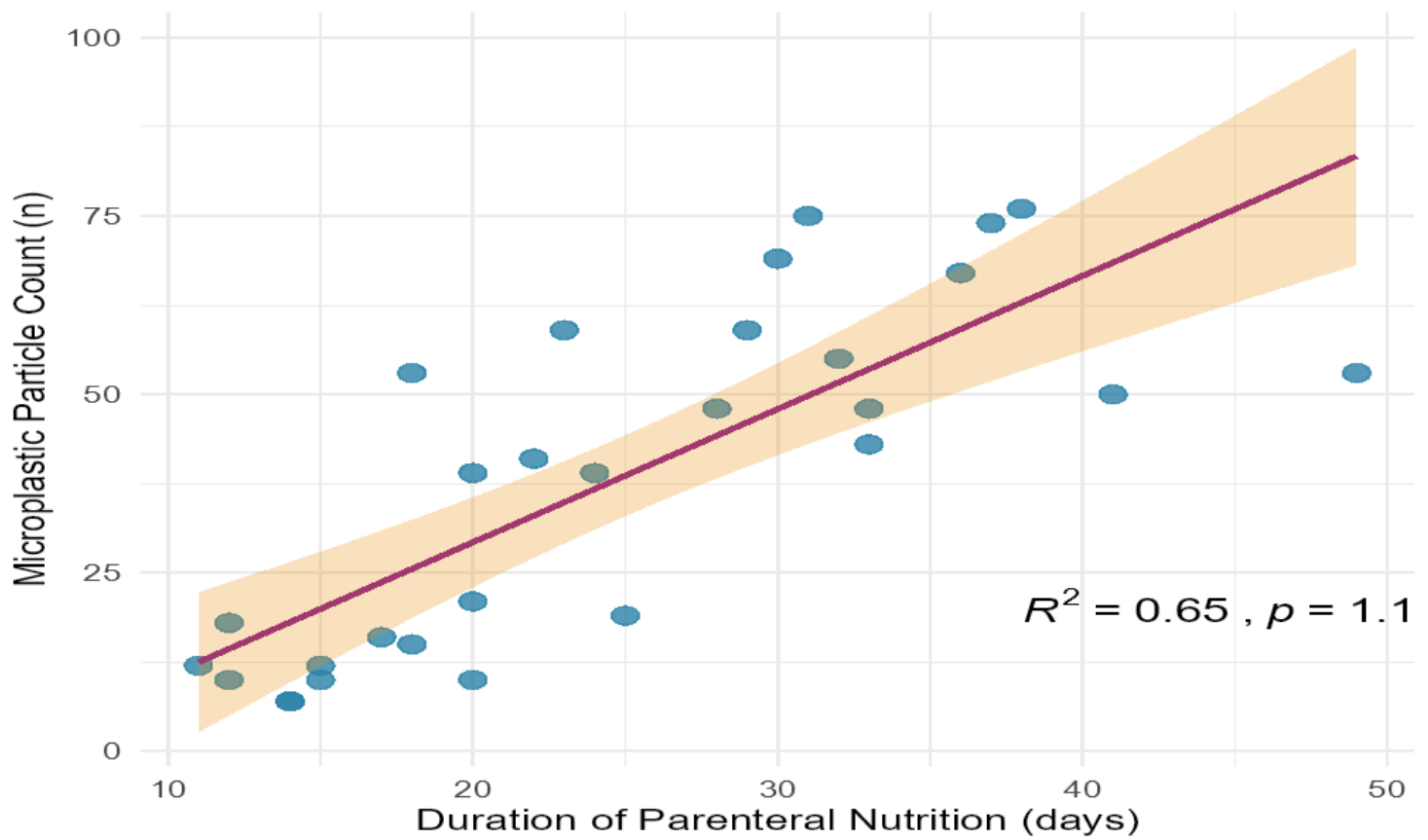


Figure 3

Association between parenteral nutrition duration and microplastic particle count. Scatter plot of PN duration (days) and MP particle count in 29 preterm infants with BPD. The solid line represents the linear regression fit and the shaded area its 95% confidence interval. Spearman's rank correlation was $r = 0.862$ ($P < 0.001$).

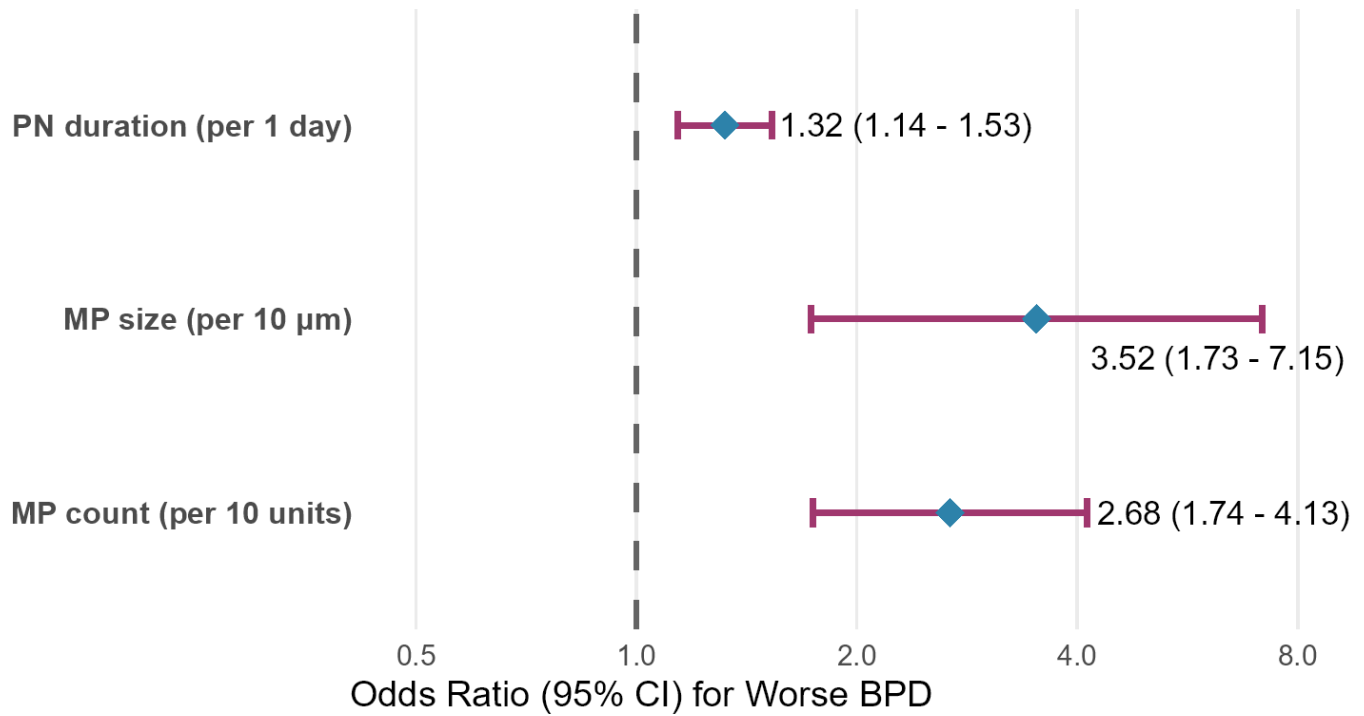


Figure 4

Ordinal logistic regression results for BPD severity. Forest plot of odds ratios (ORs) and 95% confidence intervals (CIs) for BPD severity (mild, moderate, or severe). The dashed vertical line indicates OR = 1. Separate models were constructed for PN duration (per 1-day increase), MP particle count (per 10-unit increase), and mean MP size (per 10- μm increase). PN duration: OR = 1.32, 95% CI 1.14–1.53, $P < 0.001$; MP particle count: OR = 2.68, 95% CI 1.74–4.13, $P < 0.001$; mean MP size: OR = 3.52, 95% CI 1.73–7.15, $P = 0.002$.