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Research Article

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Risk Stratification for Adverse Outcomes in Preterm Infants with a Birth Weight of Less Than 1500 G Based on Follow-Up Data

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Abstract

Objective: To compare the patterns of perinatal morbidity, morbidity during the first year of life, and disability among preterm infants with a birth weight of less than 1500 g according to their classification as extremely low birth weight or very low birth weight.

Materials and Methods: Data from the internal registry of preterm infants maintained by the Republican Center for Follow-up Care of Preterm Infants, Republican Scientific and Practical Center «Mother and Child» (Minsk, Republic of Belarus), were analyzed for 224 infants receiving follow-up care. Two groups were defined according to birth weight: extremely low birth weight (ELBW; <1000 g; n=91) and very low birth weight (VLBW; 1000–1500 g; n=133). The frequencies of pathological conditions were compared between groups. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and the Holm correction was applied for multiple comparisons.

Results: Severe central nervous system injury, congenital pneumonia, sepsis, bronchopulmonary dysplasia (BPD), and retinopathy of prematurity were more frequently recorded among infants with ELBW. During the first year of life, BPD was diagnosed in 82.4% of infants with ELBW compared with 33,1% of those with VLBW (OR=9,48; 95% CI, 4,95–18,15; p<0,001). Disability was documented in 17,6% and 3,8% of infants, respectively (OR=5,46; 95% CI, 1,92–15.51; p=0,015).

Conclusion: Preterm infants with ELBW constitute the highest-risk subgroup among infants with a birth weight of less than 1500 g. These findings support a differentiated, risk-oriented approach to the follow-up care of preterm infants.

Keywords: Preterm infants, Extremely low birth weight, Very low birth weight, Follow-up care, Registry, Disability, Risk stratification

Introduction

Preterm birth remains one of the most significant challenges in contemporary pediatrics, affecting not only neonatal morbidity and mortality but also the child's health and developmental trajectory beyond the neonatal period [1]. Advances in neonatal care, including improvements in respiratory support, intensive care, and specialized management of infants with extremely low and very low birth weight, have increased the number of children surviving critical conditions during the neonatal period. Consequently, increasing attention is being directed not only toward immediate outcomes of neonatal care but also toward the long-term consequences of preterm birth that may shape subsequent physical, neurodevelopmental, and functional outcomes [1-3].

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Infants with a birth weight of less than 1500 g constitute a population at particularly high medical risk. Organ immaturity, limited adaptive capacity, and the high prevalence of infectious and inflammatory conditions, central nervous system injury, bronchopulmonary dysplasia, retinopathy of prematurity, impaired growth, and nutritional disturbances contribute to a complex pattern of morbidity that may persist or evolve beyond the neonatal period [2-5]. However, this population is not homogeneous. The degree of immaturity and severity of the initial clinical condition differ substantially between infants with extremely low birth weight (ELBW; <1000 g) and those with very low birth weight (VLBW; 1000-1500 g), potentially resulting in distinct patterns of subsequent morbidity and differing risks of adverse outcomes [2,4,6].

In this context, structured follow-up care is of particular importance, as it enables longitudinal assessment of the child after discharge from the neonatal unit, identification of persistent or emerging impairments, timely determination of the need for specialized medical care, and evaluation of the functional consequences of perinatal morbidity. The effectiveness of follow-up care, however, depends not only on its duration but also on the ability to identify subgroups of preterm infants with different levels of clinical risk [1,4,7]. The use of registry-based data provides additional opportunities to characterize morbidity patterns and identify clinically relevant associations within large or specialized patient populations. Registries allow information on perinatal morbidity to be integrated with subsequent health outcomes, facilitate comparisons between clinically defined subgroups, and help identify characteristics associated with adverse outcomes. This approach is particularly relevant in preterm infants, as the high prevalence of individual conditions does not necessarily correspond to the likelihood of persistent functional impairment or disability [1-3,7-9].

Accordingly, an important clinical and research priority is not merely to quantify the frequency of individual conditions among infants with a birth weight of less than 1500 g, but to comprehensively characterize differences in health profiles according to birth weight. Identification of infants at greatest risk may provide a basis for developing differentiated follow-up pathways, prioritizing specific areas of medical care, and initiating interventions at an earlier stage of an unfavorable developmental trajectory [10-17].

The Aim of the Present Study

The aim of the present study was to compare the patterns of perinatal morbidity, morbidity during the first year of life, and disability among preterm infants with a birth weight of less than 1500 g according to their classification as extremely low birth weight or very low birth weight, using data from a follow-up registry.

Materials and Methods

Materials and Methods. A comparative analysis was performed using data from the internal registry of preterm infants receiving follow-up care at the Republican Center for Follow-up Care of Preterm Infants, State Institution “Republican Scientific and Practical Center “Mother and Child” (Minsk, Republic of Belarus). The study included 224 preterm infants with a birth weight of less than 1500 g. According to birth weight, the infants were divided into two groups: Group 1 comprised infants with extremely low birth weight (ELBW; <1000 g; n=91), and Group 2 comprised infants with very low birth weight (VLBW; 1000–1500 g; n=133). Infants with ELBW accounted for 40,6% of the study population, whereas those with VLBW accounted for 59,4%. This grouping enabled assessment of the heterogeneity of health status among infants with a birth weight of less than 1500 g and identification of differences in adverse outcome profiles according to the degree of reduction in birth weight.

In accordance with the study objectives, the analysis comprised two principal domains of indicators. The first domain included pathological conditions characterizing the perinatal period: infection specific to the perinatal period, congenital pneumonia, congenital sepsis, encephalopathy of prematurity, nonspecific enterocolitis, fetal growth restriction, Bronchopulmonary Dysplasia (BPD), Retinopathy of Prematurity (ROP), Anemia, Intraventricular Hemorrhage (IVH), Periventricular Leukomalacia (PVL), congenital heart defects, patent ductus arteriosus, severe brain injury, and other Central Nervous System (CNS) disorders.

The second domain characterized health status during the first year of life and included CNS disorders, BPD, ophthalmologic disorders, anemia, hearing impairment, protein-energy malnutrition, and disability. Vaccination coverage during the first and second years of life was additionally assessed. The selection of indicators reflected the principal areas of medical follow-up of preterm infants and the availability of corresponding variables in the registry database.

For each indicator, the absolute number of affected infants and the corresponding proportion within each study group were determined. Relative frequencies were expressed as percentages calculated using the number of infants in the respective group as the denominator. Between-group differences in the frequency of the studied conditions were assessed for infants with ELBW and VLBW.

Disability documented during the follow-up period was defined as the primary clinically relevant adverse outcome. Additional pathological conditions potentially associated with the development of persistent functional impairment were analyzed, including severe brain injury, IVH, PVL, CNS disorders, BPD, and ROP. This approach enabled comparison of the pattern of perinatal morbidity with subsequent health status and identification of

indicators associated with the most pronounced differences between the study groups. Statistical analysis was performed using methods appropriate for categorical variables. Frequencies were compared using Pearson's chi-square test when the assumptions for its application were met. Fisher's exact test was used when expected cell counts were small, including situations in which a small number of observations occurred in one or more cells of a 2×2 contingency table.

The strength of the association between ELBW status and the studied outcomes was quantified using odds Ratios (ORs) with 95% Confidence Intervals (CIs). An OR greater than 1 was interpreted as indicating higher odds of the respective outcome among infants with ELBW compared with those with VLBW. Interpretation of the estimates took into account both the magnitude of the OR and the precision of the estimate, as reflected by the width and position of the 95% CI relative to unity. Because multiple clinical indicators were assessed simultaneously, the Holm procedure was applied to control the risk of false-positive findings arising from multiple comparisons. A two-sided adjusted p value <0,05 was considered statistically significant. Fisher's exact test was preferentially used for outcomes with small numbers of observations. This approach reduced the likelihood of interpreting isolated differences attributable to sparse data as statistically robust associations.

The interpretation of statistical findings took into account the observational nature of the registry-based study. The observed differences and associations were considered indicators of different levels of risk within the study population and were not interpreted as evidence of a causal effect of birth weight on the development of a specific disease or outcome. The findings were used to identify clinically relevant areas for risk stratification and to support a differentiated approach to follow-up care. Statistical significance was assessed with consideration of both absolute differences in the frequency of the studied conditions and the magnitude of the ORs with their corresponding 95% CIs. Conclusions were based primarily on associations that remained statistically significant after adjustment for multiple comparisons.

Results and Discussion

Comparative analysis demonstrated substantial heterogeneity in the pattern of perinatal morbidity and health status according to birth weight. Analysis of the pattern of perinatal morbidity revealed the most pronounced between-group differences in central nervous system injury and respiratory morbidity. Intraventricular hemorrhage (IVH) was recorded in 20 (22,0%) infants with ELBW compared with only 3 (2,3%) infants with VLBW. The odds of IVH were 12,2-fold higher among infants with ELBW than among those with a birth weight of 1000–1500 g (OR=12,21; 95% CI, 3,51–42,50; p<0.001 after adjustment for multiple comparisons). Severe brain injury was identified in 13 (14,3%) infants with ELBW and 2 (1,5%) infants with VLBW. ELBW status was associated with substantially higher odds of severe brain injury (OR=10,92; 95% CI, 2,40–49,66; p=0,005 after the Holm adjustment).

Periventricular Leukomalacia (PVL) was also more frequent among infants with ELBW than among those with VLBW (15,4% vs 4,5%). Although the unadjusted between-group difference was statistically significant (p=0,008), statistical significance was not maintained after adjustment for multiple comparisons (adjusted p=0,114) (Table 1). p values are adjusted using the Holm correction for multiple comparisons. OR >1 indicates higher odds of the respective condition or outcome in the ELBW group compared with the VLBW group. y dysplasia; OR, odds ratio; CI, confidence interval.

Table 1: Frequency of major pathological conditions and adverse outcomes in infants with ELBW and VLBW.

Indicator	ELBW, n=91	VLBW, n=133	OR (95% CI)	p*
Congenital pneumonia	44 (48,4%)	30 (22,6%)	3,21 (1,80-5,73)	0,002
Sepsis	17 (18,7%)	6 (4,5%)	4,86 (1,84-12,88)	0,023
Fetal growth restriction	45 (49,5%)	39 (29,3%)	2,36 (1,35-4,11)	0,052
BPD, perinatal period	38 (41,8%)	25 (18,8%)	3,10 (1,70-5,66)	0,005
Retinopathy of prematurity	40 (44,0%)	32 (24,1%)	2,48 (1,39-4,39)	0,040
Intraventricular hemorrhage	20 (22,0%)	3 (2,3%)	12,21 (3,51-42,50)	<0,001
Periventricular leukomalacia	14 (15,4%)	6 (4,5%)	3,85 (1,42-10,43)	0,114
Severe brain injury	13 (14,3%)	2 (1,5%)	10,92 (2,40-49,66)	0,005
Nervous system disorders, first year of life	75 (82,4%)	91 (68,4%)	2,16 (1,13-4,15)	0,284
Ophthalmologic disorders	79 (86,8%)	104 (78,2%)	1,84 (0,88-3,82)	1,000
BPD, first year of life	75 (82,4%)	44 (33,1%)	9,48 (4,95-18,15)	<0,001
Anemia, first year of life	67 (73,6%)	90 (67,7%)	1,33 (0,74-2,41)	1,000
Protein-energy malnutrition	19 (20,9%)	10 (7,5%)	3,25 (1,43-7,36)	0,071
Disability	16 (17,6%)	5 (3,8%)	5,46 (1,92-15,51)	0,015

Infectious and inflammatory morbidity also differed substantially between the groups. Congenital pneumonia was diagnosed in 44 (48,4%) infants with ELBW and in 30 (22,6%) infants with VLBW. The odds of congenital pneumonia were more than threefold higher in the ELBW group (OR=3,21; 95% CI, 1,80–5.73; p=0,002 after adjustment). Sepsis was diagnosed in 17 (18,7%) and 6 (4,5%) infants, respectively, with an OR of 4.86 (95% CI, 1,84–12,88; p=0,023 after adjustment). BPD during the perinatal period was also more frequently recorded among infants with ELBW than among those with VLBW: 38 (41,8%) versus 25 (18,8%), respectively. The odds of BPD were 3,1-fold higher in the ELBW group (OR=3,10; 95% CI, 1,70–5,66; p=0,005).

Retinopathy of prematurity was diagnosed in 40 (44,0%) infants with ELBW and 32 (24,1%) infants with VLBW. The between-group difference remained statistically significant after adjustment for multiple comparisons (OR=2,48; 95% CI, 1,39–4,39; p=0,040). Fetal growth restriction was observed in 45 (49,5%) infants with ELBW and 39 (29,3%) infants with VLBW. Although the unadjusted difference was statistically significant (p=0,003), statistical significance was not maintained after application of the Holm correction (adjusted p=0,052). A similar pattern was observed for protein-energy malnutrition during the first year of life, which occurred in 20,9% of infants with ELBW compared with 7,5% of those with VLBW; the unadjusted p value was 0,004, whereas the adjusted p value was 0,071.

Analysis of indicators reflecting the health status of preterm infants showed that substantial between-group differences in morbidity persisted throughout the first year of life. The most pronounced difference was observed for BPD. During the first year of life, BPD was recorded in 75 (82,4%) infants with ELBW compared with 44 (33,1%) infants with VLBW. ELBW status was associated with an almost tenfold increase in the odds of BPD during the first year of life (OR=9,48; 95% CI, 4,95–18,15; p<0,001 after adjustment). Nervous system disorders remained among the most prevalent components of morbidity during the first year of life. Various forms of nervous system involvement were recorded in 75 (82,4%) infants with ELBW and 91 (68,4%) infants with VLBW. These findings indicate a high burden of neurological morbidity in both groups, although its absolute frequency was higher among infants with ELBW. Within this domain, the most pronounced difference concerned severe brain injury, the frequency of which was almost tenfold higher in the ELBW group than in the VLBW group.

Ophthalmologic disorders were also highly prevalent in both groups, affecting 79 (86,8%) infants with ELBW and 104 (78,2%) infants with VLBW. Despite the high prevalence, no statistically significant between-group difference was identified (p=0,115). This finding suggests that the need for ophthalmologic follow-up is relevant across the entire population of infants with a birth weight of less than 1500 g and should not be regarded solely as a risk characteristic specific to ELBW. Anemia was likewise common in both groups, occurring in 67 (73,6%) infants with ELBW and 90 (67,7%) infants with VLBW. The difference was not statistically significant (OR=1,33; 95% CI, 0,74–2,41; p=0,375). Thus, the high prevalence of anemia characterizes both groups and warrants attention as part of follow-up care irrespective of birth weight category.

The most clinically relevant between-group difference was observed for disability. During the follow-up period, disability was documented in 16 (17,6%) infants with ELBW compared with 5 (3,8%) infants with VLBW, corresponding to an absolute difference of 13,8 percentage points. ELBW status was associated with more than fivefold higher odds of disability compared with VLBW (OR=5,46; 95% CI, 1,92–15,51). This difference remained statistically significant after adjustment for multiple comparisons (p=0,015). The findings demonstrate substantial heterogeneity in health status among infants with a birth weight of less than 1500 g. Although all infants in the study represented a population at very high perinatal risk, a birth weight below 1000 g was associated with a substantially higher frequency of several pathological conditions of particular relevance to subsequent development. After adjustment for multiple comparisons, the most robust between-group differences were observed for IVH, severe brain injury, BPD, congenital pneumonia, sepsis, ROP, and disability.

The magnitude of the differences in central nervous system injury is particularly noteworthy. IVH occurred in 22,0% of infants with ELBW compared with 2,3% of those with VLBW, while severe brain injury was documented in 14,3% and 1,5%, respectively. These findings are consistent with a population-based cohort study by Pascal et al., in which IVH and PVL were associated with an increased risk of adverse neurodevelopmental outcomes in very preterm and very low birth weight infants [10]. The concentration of severe cerebral pathology among infants with ELBW identified in our registry therefore has both diagnostic and prognostic relevance and supports early neurological risk stratification in this population.

The findings concerning PVL warrant a cautious interpretation. Although PVL was more frequent among infants with ELBW than among those with VLBW (15,4% vs 4,5%) and the unadjusted difference was statistically significant, this association did not remain statistically significant after adjustment for multiple comparisons. Accordingly, PVL cannot be considered an independently statistically supported marker distinguishing the two groups within the present sample. Nevertheless, its clinical relevance remains important given its potential association with adverse neurodevelopmental outcomes reported in contemporary studies [10].

This finding illustrates the importance of distinguishing statistical significance from clinical significance when interpreting registry-based data. Respiratory morbidity represented the second major domain of between-group differences. During the first year of life, BPD was diagnosed in 82,4% of infants with ELBW and 33,1% of those with VLBW, with almost tenfold higher odds in the former group. The high prevalence of BPD among very low birth weight

infants is consistent with contemporary systematic reviews, while the severity of BPD has been associated with subsequent adverse respiratory and neurodevelopmental outcomes [12,14,15]. Our findings indicate that the difference between the groups is already evident during the perinatal period and persists after discharge from neonatal care, supporting the consideration of BPD as one of the most informative components of the high-risk profile in infants with ELBW. An important consideration is that contemporary literature increasingly regards BPD not only as a chronic respiratory disorder but also as a potential marker of broader adverse outcomes in extremely preterm infants. Baud et al. demonstrated the potential utility of BPD for predicting neurodevelopmental impairment in infants born extremely preterm [13].

In our study, BPD was substantially concentrated in the ELBW group, suggesting that it may represent one component of a multidimensional risk-stratification framework. However, the present findings do not establish a causal role of BPD in the development of disability. Infectious and inflammatory morbidity was also more frequent among infants with ELBW. Congenital pneumonia occurred in nearly half of the infants in this group, while sepsis affected approximately one in five. A similar pattern has been reported in studies of outcomes among very low birth weight infants. In particular, Battajon et al. demonstrated an association between sepsis and subsequent adverse neurodevelopmental outcomes in VLBW infants [6]. Thus, infectious morbidity, in combination with severe CNS injury and BPD, may be considered a component of a multidimensional adverse-outcome profile that is particularly pronounced among infants with ELBW.

At the same time, the present findings demonstrate that a high prevalence of a particular condition does not necessarily imply a statistically significant difference between groups. Ophthalmologic disorders were observed in 86,8% of infants with ELBW and 78,2% of those with VLBW, while anemia occurred in 73,6% and 67,7%, respectively. Despite their high prevalence, neither condition differed significantly between the groups. This distinction suggests that the conditions assessed in the present study may be broadly categorized into those whose prevalence increases substantially with ELBW and may therefore contribute to risk stratification, and those that are common throughout the population of infants with a birth weight of less than 1500 g and consequently warrant inclusion in universal follow-up care.

This distinction is particularly relevant to ROP. In our study, ROP was significantly more frequent among infants with ELBW, whereas ophthalmologic disorders as a broader category were highly prevalent in both groups. Data from a nationwide cohort study by Ahn et al. demonstrated an association between ROP and subsequent neurodevelopmental outcomes in VLBW infants [11]. Accordingly, ophthalmologic surveillance should be regarded not only as a specialized component of eye care but also as an integral part of comprehensive developmental follow-up.

The most clinically significant finding of the present study was the between-group difference in disability. Disability was documented in 17,6% of infants with ELBW compared with only 3,8% of those with VLBW, with 5,46-fold higher odds in the ELBW group. Thus, the differences observed in the distribution of individual pathological conditions were reflected in a clinically meaningful endpoint. Nevertheless, the present data do not support considering birth weight as the sole determinant of disability. Rather, birth weight may be viewed as an integrated marker of the degree of immaturity and severity of the perinatal condition, associated with a constellation of factors that shape subsequent health trajectories. An important finding is the contrast between the high prevalence of individual conditions and the relatively low frequency of disability among infants with VLBW. Despite nervous system disorders being documented in 68,4% and ophthalmologic disorders in 78,2% of these infants, disability was recorded in only 3,8%. This suggests that the presence of an individual disease does not necessarily equate to the development of persistent functional limitation. Accordingly, the purpose of follow-up care extends beyond diagnostic surveillance to include timely identification of functional impairments, assessment of their trajectory, and prevention of potentially reversible conditions from progressing to persistent disability.

The findings support a risk-oriented approach to follow-up care. Infants with ELBW should be regarded as a priority population requiring early and comprehensive assessment of neurological, respiratory, ophthalmologic, and nutritional status. Contemporary evidence emphasizes the importance of early detection of developmental delay in infants born very preterm or with very low birth weight, thereby creating an opportunity for timely intervention [16]. In this context, registry-based risk stratification may facilitate a transition from a uniform follow-up model toward differentiated care pathways tailored to individual risk profiles. An important advantage of registry-based follow-up is the ability to integrate information on perinatal morbidity with subsequent health outcomes. Previous studies based on this registry have demonstrated its utility for analyzing the structure of morbidity during the first year of life, maternal factors associated with preterm birth, and associations between maternal pathology and morbidity in preterm infants [1–3]. The present study extends this approach by shifting the focus from descriptive characterization of morbidity to comparative assessment of the risk of adverse outcomes according to birth weight.

The findings support the use of a birth weight below 1000 g as a clinically meaningful criterion for identifying the highest-risk subgroup within the population of infants with a birth weight of less than 1500 g. However, birth weight should not be considered the sole prognostic indicator. A multidimensional risk-stratification model incorporating birth weight together with the most clinically relevant perinatal characteristics – particularly severe CNS injury, BPD, infectious morbidity, and other factors associated with adverse outcomes – represents a promising direction for further research.

Conclusion

Preterm infants with a birth weight of less than 1500 g constitute a heterogeneous population in terms of the risk of adverse outcomes. Infants with ELBW demonstrated a higher frequency of severe perinatal morbidity, particularly IVH, severe brain injury, sepsis, congenital pneumonia, BPD, and ROP. During the first year of life, infants with ELBW continued to demonstrate a greater burden of clinically significant morbidity, with BPD showing the most pronounced between-group difference: 82,4% versus 33,1% among infants with VLBW (OR=9,48; 95% CI, 4,95–18,15; p<0.001). ELBW was associated with substantially higher odds of disability: 17.6% versus 3.8% among infants with VLBW (OR=5,46; 95% CI, 1,92–15,51; p=0,015). These findings support the use of a birth weight below 1000 g as a clinically meaningful criterion for identifying infants at particularly high risk of adverse outcomes. The registry-based findings support a differentiated, risk-oriented approach to the follow-up care of preterm infants with a birth weight of less than 1500 g, with prioritized follow-up of infants with ELBW and early assessment of neurological, respiratory, ophthalmologic, and nutritional impairments. Ethics approval and informed consent. The study was approved by the Ethics Committee of the Republican Scientific and Practical Center «Mother and Child». Written informed consent was obtained from the parents or legal representatives of all participants.

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Conflict of interest

Conflict of interest. The authors declare no conflict of interest.

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