Scientific Reports

https://doi.org/10.1038/s41598-026-53670-6

Article in Press

Assessment of survival and neonatal morbidity rates of very low birth weight infants in Türkiye: Turkish Neonatal Society SECRETS (TNS-SECRETS) study

Received: 18 March 2026

Accepted: 13 May 2026

Published online: 29 May 2026

Cite this article as: Cetinkaya M., Memur S., Koc E. *et al.* Assessment of survival and neonatal morbidity rates of very low birth weight infants in Türkiye: Turkish Neonatal Society SECRETS (TNS-SECRETS) study. *Sci Rep* (2026). https://doi.org/10.1038/s41598-026-53670-6

M. Cetinkaya, S. Memur, E. Koc, A. Y. Bas & Turkish Neonatal Society SECRETS Study Group

We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

If this paper is publishing under a Transparent Peer Review model then Peer Review reports will publish with the final article.

ARTICLE IN PRESS

© The Author(s) 2026. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

ARTICLE IN PRESS

Title: Assessment of Survival and Neonatal Morbidity Rates of Very Low Birth Weight Infants in Türkiye: Turkish Neonatal Society SECRETS (TNS-SECRETS) Study

Authors: Cetinkaya M[1,2*], Memur S[1], Koc E[3], Bas AY[4], Turkish Neonatal Society SECRETS Study Group

Affiliations

[1] Division of Neonatology, Department of Pediatrics, Health Sciences University, Basaksehir Cam Sakura City Hospital, Istanbul, Türkiye

[2] Division of Neonatology, Department of Pediatrics, Istanbul Atlas University, Faculty of Medicine, Istanbul, Türkiye

[3] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Gazi University, Ankara, Türkiye

[4] Division of Neonatology, Department of Pediatrics, Yildirim Beyazit University, Ankara, Türkiye

***Corresponding Author:**

Merih Cetinkaya

Adress: Division of Neonatology, Department of Pediatrics, İstanbul Atlas University, Kagıthane, Istanbul, Turkiye.

Postal Code:34408

Email: drmerih@yahoo.com

Telephone: +90 532 3678867

ARTICLE IN PRESS

ARTICLE IN PRESS

Assessment of Survival and Neonatal Morbidity Rates of Very Low Birth Weight Infants in Türkiye: Turkish Neonatal Society SECRETS (TNS-SECRETS) Study

Abstract

This prospective multicenter study of the Turkish Neonatal Society includes data from a large cohort of very low birth weight (VLBW) infants from 78 referral centers in Türkiye. The objective was to evaluate survival and neonatal morbidity rates among VLBW infants. All preterm infants with a birth weight (BW) ≤1500 grams and a gestational age (GA) between $23^{0/7}$ and $31^{6/7}$ weeks were included. Respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL) hemodynamically significant patent ductus arteriosus (hsPDA), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), sepsis and retinopathy of prematurity (ROP) were defined as neonatal morbidities. A total of 3042 VLBW infants were enrolled. The mean GA and median BW were 27 ± 2.2 weeks and 1080 g (ranges, 320 and 1500 g), respectively. The incidences of neonatal morbidities were as follows: RDS 76.3%, IVH 28%, PVL 0.9%, hsPDA 31.5%, BPD 39.5%, NEC 14%, and ROP 25%. Early and late sepsis were diagnosed in 19.3% and 44.6% of the study group. The overall mortality rate was 21.7%, and survival without major morbidity was 42.8%. Mortality among infants ≤28 weeks of gestation was 34.8%, whereas it was 5.5% for infants >28 weeks of GA. This study provides a comprehensive overview of outcomes among VLBW infants in Türkiye and offers valuable

ARTICLE IN PRESS

insights for other developing countries. As neonatal morbidity and mortality rates remain higher than those reported in developed countries, targeted strategies to improve neonatal care practices for extremely preterm infants should be prioritized.

Key words: extremely premature infant, neonatal morbidity, preterm infant, survival, very low birth weight infant

Introduction

Preterm birth (PTB) remains the leading cause of neonatal morbidity and mortality worldwide and is also a major contributor to childhood mortality. The risks of mortality and neonatal morbidities are inversely related to gestational age (GA) and birth weight (BW). According to recent estimates, 20–30 million small and sick newborns require hospitalization annually, nearly half of whom are preterm infants. Furthermore, approximately 2.3 million infants die annually during the neonatal period, with prematurity-related complications accounting for the majority of deaths. Nearly all neonatal deaths (98%) occur in low- and middle-income countries (LMICs). Therefore, mortality among very low birth weight (VLBW) and extremely low birth weight (ELBW) infants remains high especially in developing countries, with outcomes strongly influenced by GA and the availability of healthcare resources. In addition, the burden of major neonatal morbidities remains substantial, and survival without significant morbidity is uncommon among survivors, particularly in infants born at lower GAs. Although the most recent global PTB rate was estimated at approximately

ARTICLE IN PRESS

9.9% in 2020, the rate has been reported to be substantially higher as around 15% in Türkiye [1-5].

Despite advances in perinatal and neonatal care and the establishment of high-technology neonatal intensive care units (NICUs), certain major morbidities including intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), hemodynamic significant patent ductus arteriosus (hsPDA), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), sepsis and retinopathy of prematurity (ROP) continue to occur among survivors. These conditions are associated with prolonged hospitalization, adverse short and long-term outcomes, and increased healthcare costs in high-risk infants [6]. Consequently, improving the quality of care for preterm infants and reducing prematurity-related mortality and morbidities require adherence to national and international guidelines, implementation of evidence-based preventive and therapeutic practices, and provision of parental support measures [4].

In recent years, Türkiye has undertaken extensive perinatal and neonatal healthcare initiatives to enhance neonatal survival and outcomes. Collaborative strategies developed by the Turkish Ministry of Health and the Turkish Neonatal Society (TNS) included strengthening NICU standards, conducting quality-improvement programs, expanding specialized neonatal transport services, training of NICU healthcare professionals, and establishing modern high-intensity NICUs for critically ill newborns. Additional efforts have focused on structured antenatal follow-up,

ARTICLE IN PRESS

standardizing delivery room (DR) practices, implementing Neonatal Resuscitation Programme (NRP) training, developing national TNS guidelines, and promoting breastfeeding and baby-friendly healthcare initiatives. As a result, neonatal mortality rates declined sharply between 2000 and 2011 but have remained stable since the early 2010s [7-9].

Strengthening national data systems is essential to improve the availability of individual-level data for clinical practice, policy implementation, and quality improvement initiatives in maternity wards and NICUs. When combined with structured follow-up programs, these systems have been proposed as a key strategy for achieving Sustainable Development Goal (SDG) 3.2 and the Every Newborn Action Plan, which both aim to eliminate preventable neonatal and under-5 mortality, specifically targeting a neonatal mortality rate of ≤ 12 per 1,000 live births in every country [1].

ARTICLE IN PRESS

Although several small center-based studies exist, there is very limited data on the survival and neonatal morbidity rates for VLBW infants in Türkiye. The lack of local nationwide information limits evaluation of NICU performance, identification of gaps in preterm care practices and results with uniformity in clinical decision-making. It also hinders meaningful comparisons of national outcomes with international benchmarks. The objective of this prospective multicenter study was to determine survival and neonatal morbidity rates among VLBW infants who either died during hospitalization or were discharged from NICUs across Türkiye.

Results

ARTICLE IN PRESS

A total of 3386 preterm infants with BW ≤1500 grams and GA of $23^{0/7}$ weeks to $31^{6/7}$ weeks were hospitalized in 78 NICUs during the study period, 3042 (89.8%) eligible infants were included in the study. Of these, 1464 (48%) were male, and 2629 (86%) of them were appropriate for GA (AGA). The mean GA and median BW of infants were 27 ± 2.2 weeks and 1080 (ranges, 320 to 1500) grams, respectively. The number of multiple births was 743(24%). A total of 2650 infants (87%) were born by cesarean sectio and 97 (3.2%) infants were outborn. The mean maternal age was 29.2 ± 5 years, and 47% of mothers were primigravida. Maternal diseases were present in 38% of pregnant women, and 74% of them had at least one antenatal visit. Any dose of antenatal corticosteroid (ACS) therapy was administered in 2207 (72.5%) pregnant women. Table 1 shows both neonatal and maternal characteristics of the study group.

Table 2 shows the DR and NICU practices in the study group in terms of GA. Neonatal resuscitation in the DR including positive pressure ventilation, chest compression, intubation, and adrenalin was administered in 1823 (59.9%), 1177(38.6%), 99 (3.2%) and 40(1.3%) infants, respectively. A total of 656 (21.5%) infants had delayed cord clamping (DCC) between 30 to 60 seconds. Intratracheal surfactant was administered in 2111 infants (69.3%). Among those, 188 infants (6.2%) received prophylactic surfactant therapy in the DR, 1573 infants (51.7%) received rescue surfactant therapy in the NICU and 350 infants (11.5%) received surfactant in both DR and NICU. Surfactant was administered by less invasive surfactant

ARTICLE IN PRESS

administration (LISA) or minimally invasive surfactant therapy (MIST) in 296 infants (9.7%) whereas the remaining received it by INtubation-SURfactant-Extubation (INSURE) technique. Initially, non-invasive, invasive and high frequency mechanical ventilation (MV) were required in 49%, 49%, and 2% of infants, respectively. Systemic and inhaled postnatal corticosteroids were applied in 677 (22.5%) and 360 (11.8%) infants, respectively. Caffeine therapy was administered in 89% (2709 of 3042) of infants, with a median duration of 36 days. Total parenteral nutrition (TPN) was started in 96.3% of all infants and the median duration of TPN was 12 days. Oropharyngeal mother's milk (OMM) was administered to 744 infants (24.5%) within the first 72 hours of life and to 44 infants (1.4%) after 72 hours of life. Minimal enteral nutrition (MEN) was established in 1348 infants (44.3%) within the first 24 hours and in 1131 infants (37.1%) after 24 hours. The infants reached full enteral nutrition and full oral feeding in a median of 19 and 49 days, respectively. The median duration of hospitalization were 56 and 18 days among survivors and non-survivors, respectively.

ARTICLE IN PRESS

The incidences of respiratory outcomes including respiratory distress syndrome (RDS) and BPD were 76.3% and 39.5%, respectively. NEC, ROP and hsPDA were diagnosed in 14%, 25%, and 31.5% of infants, respectively. Any stage of IVH, severe IVH and PVL were detected in 28%, 8.7 and 0.9% of the study group, respectively. Early and late sepsis were diagnosed in 19.3% and 44.6% of the infants. Table 3 shows the incidences of neonatal morbidities in the study population with respect to GA.

ARTICLE IN PRESS

The overall mortality rate in the study cohort was 21.7% as 661 infants died. The survival rate without major morbidity was 42.8%. The early, late and post-neonatal mortality rates were 12.7%, 6.2% and 2.9%, respectively. Table 4 shows the survival without major morbidity and mortality rates of the study cohort. Subgroup analysis showed that mortality was 34.8% (585/1,679) among infants born at ≤28 weeks' GA compared with 5.5% (76/1,363) among those born at >28 weeks of gestation. GA was significantly associated with mortality, as infants born at ≤28 weeks' GA had markedly higher risk of death than those born at >28 weeks' GA (χ^2 = 378.86, p <0.001), also consistent with Fisher's exact test (p <0.001). Infants born at ≤28 weeks' GA exhibited an approximately 9-fold increased risk of mortality compared to those born at >28 weeks' GA (OR: 9.06; 95% CI: 7.04–11.65). Comparison of both survival and survival without major morbidities of the study group in terms of GA is shown in Figure 1.

ARTICLE IN PRESS

The multivariate logistic regression analysis identified several independent predictors for mortality and major morbidities among infants born at ≤28 weeks' GA. Lower GA (per 1-week decrease), lower BW (per 100-g decrease), prolonged MV during the first 7 days of life, and neonatal sepsis were significantly associated with increased risks of mortality, NEC, and severe IVH. In contrast, exposure to ACS therapy was independently associated with reduced risks of these outcomes. Male sex was not identified as an independent risk factor for mortality and any of major morbities

ARTICLE IN PRESS

assessed. Table 5 shows the multivarite logistic regression analysis for mortality, NEC, and severe IVH in infants born ≤28 weeks of GA.

Discussion

This is the largest prospective multicenter study to date, encompassing 3,042 VLBW infants across 78 Level III and IV NICUs in Türkiye, where neonatologists serve as primary staff. By establishing comprehensive baseline data on survival and neonatal morbidities stratified by GA, our findings provide an important national benchmark. These results provide a framework for developing healthcare strategies and quality improvement initiatives to optimize neonatal care for very preterm infants in Türkiye. Furthermore, this approach may serve as a model for other developing countries to improve national neonatal care standards.

It is well known that PTB and prematurity-related complications constitute the leading cause of death in children < 5 years. Consequently, preventing PTB rates is a global priority to reduce associated morbidities and improve survival [10]. Notably, extremely preterm infants contribute disproportionately to both neonatal mortality and childhood morbidity, despite recent advances in neonatal clinical practice [11]. In addition, these conditions are also associated with adverse long term health outcomes among those who survive. Therefore, efforts to reduce PTB rates are essential not only for global health improvement but also for the long-term economic and social stability of developing countries [12].

ARTICLE IN PRESS

Comprehensive national data on preterm infant morbidity and mortality are essential for establishing real-time monitoring, identifying care deficiencies, and facilitating quality improvement. Such data enable institutions to benchmark clinical performance, optimize health service delivery, and support evidence-based clinical decision-making [13]. While several global and national prematurity-related outcomes have been published [10–17], national data within the context of Türkiye remain limited [5]. To address this empirical gap, we conducted the present prospective multicenter study to evaluate neonatal outcomes and provide a framework for standardizing care.

Administering ACS therapy and performing DCC are essential strategies for reducing PTB related complications and improving neonatal survival [18]. Evidence indicates that a single course of ACS therapy promotes fetal lung maturation and decrease the risk of perinatal death, neonatal death, RDS, and IVH in pregnancies at risk of preterm delivery [19]. ACS administration rates in developing countries typically range from 85% to 95% [20–22]. The 73% rate observed in this study, though lower than international cohorts, reflects a markedly increase trend from the 42.9% reported previously [5]. The increase in ACS therapy rates may reflect the growing awareness of obstetricians and perinatologists regarding its clear benefits for preterm infant survival. Nevertheless, despite recent improvements, further efforts are required to reach higher ACS therapy rates to achieve more favorable neonatal outcomes.

ARTICLE IN PRESS

DCC has been shown to reduce the risk of mortality before discharge in preterm infants. However, the DCC rate in our study (21.3%) was markedly lower than the rates reported in the US (81.7%) and LMICs (60%) [23,24]. As with ACS therapy, expanding DCC implementation in Turkish NICUs is essential for improving VLBW infant care and survival.

DR interventions are nearly universal in extremely preterm infants. In this cohort, 59% of neonates required stabilization and 3.2% required full CPR, reflecting trends observed in the international literature. Such early interventions are critical, as they significantly improve neonatal outcomes and survival in preterm infants [25].

RDS is an important cause of mortality in preterm infants. The incidence of RDS is inversely related to GA and BW. It affects about 80% of neonates born at 28 weeks GA and 90% of infants at 24 weeks GA. In addition, about 50-60% of RDS cases require surfactant administration [26]. RDS was diagnosed in 2324 infants (76.3%) and intratracheal surfactant was administered in 2111 infants (69.3%). Regarding surfactant administration, 51.7% of the infants received rescue therapy in the NICU, while a smaller proportion (6.2%) received prophylactic treatment in the DR; overall 11.5% of the cohort required surfactant in both settings. Our findings indicate that extremely preterm infants (GA ≤28 weeks) were significantly more likely to receive surfactant in both the DR and NICU compared to more mature infants (GA >28 weeks). Surfactant was delivered via less- or minimally-invasive methods in 9.7% of cases. The rates of LISA/MIST was lower than the

ARTICLE IN PRESS

incidence reported from Europe [27]. This discrepancy may be attributed to variations in study populations and regional or institutional care practices.

The incidence of BPD varies depending on several factors, including NICU practices and differences in the clinical definitions of BPD. The incidence of BPD in VLBW infants has remained stable at approximately 40-45% over the last few decades [28,29]. Similar to those data, the BPD rate was 39.5% in the present study. However, the Swiss Neonatal Network (SNN) and US members of the Vermont Oxford Network (US-VON) reported chronic lung disease as 25.9% and 11.8%, respectively, in survived VLBW infants [30]. Despite the mortality rate being higher in infants <28 weeks of gestation, the survivors also have higher BPD rates in our patient population. Therefore, antenatal and postnatal preventive measures and effective protocols should be implemented to reduce the risk of BPD at NICUs in Türkiye.

ARTICLE IN PRESS

Current evidence suggests that a synergistic combination of TPN and enteral nutrition during the early postnatal transition is essential to ensure adequate nutrient delivery, support optimal growth, and improve neonatal outcomes in VLBW infants. Consequently, the early initiation of TPN in combination with enteral feeding, prioritizing mothers' own milk, particularly colostrum, has become an established standard of care for preterm infants [31]. MEN was initiated within the first 24 hours of life in 44% of infants, while 37% started after 24 hours; notably, 19% of infants never received MEN in our cohort. Furthermore, despite near-universal initiation of TPN (96%),

ARTICLE IN PRESS

there was a striking lack of OMM administration in 74% of cases. These suboptimal rates of MEN and OMM utilization may be attributed to some systemic limitations in healthcare staffing, specifically the lack of specialized nutritionists and dietitians within routine NICU care in Türkiye. Consequently, our findings underscore an urgent need for standardized nutritional protocols that prioritize early MEN with OMM and the promotion of breastfeeding. Implementing such standardized practices is essential to enhance survival, reduce the incidences of NEC and neonatal sepsis and also to improve neonatal outcomes.

The reported incidence of NEC in preterm infants with a GA <32 weeks differs between 2-10%, and 5% to 22% among those with a BW<1000 g in developed countries [32]. The incidence of NEC and advanced NEC (stage ≥II) in the present study was 14% and 8.1%, respectively. These relatively high rates may be attributable to the lower use of ACS therapy, together with suboptimal nutritional and clinical care practices, including especially the limited use of MEN with OMM during the early neonatal period. The incidence of late-onset sepsis (LOS) has been reported to range between 15% and 25% among VLBW infants in developed countries [33]. In a previous multicenter study conducted in Türkiye, the incidence of LOS was 42.4% among VLBW infants [5]. Similarly, LOS was diagnosed in 44.6% of the study cohort. The higher rates of LOS and NEC may be reduced through strict adherence to infection prevention and control measures, including judicious antibiotic use, appropriate hand hygiene practices, increased awareness

ARTICLE IN PRESS

among healthcare professionals, promotion of breastfeeding, and avoidance of overcrowding in NICUs.

The frequency of PDA among VLBW infants has been reported to be 36% and 38% in Japan and Canada, respectively [34]. In the present study, the overall rate of hsPDA was 31.5%. In a previous multicenter study conducted in Türkiye, moderate-to-large PDA was reported in 46% of infants born between $24^{0/7}$ and $28^{6/7}$ weeks of GA [35]. This difference may be attributable to variations in PDA diagnostic criteria, as well as improvements in postnatal care practices in recent years.

ROP still remains a critical morbidity in both high- and middle-low-income countries, driven by the degree of immaturity and the quality of neonatal intensive care. In recent years, the reported incidence of ROP has ranged from 10% to 40%, reflecting significant variations across different nations and study populations [36]. A multicenter TR-ROP study from Türkiye reported any stage of ROP as 27% in VLBW infants [37]. Similarly, any stage of ROP in our study was detected in 25% of all infants. The slight decrease in ROP rates may also be attributable to improvements in antenatal and postnatal care over time. In our cohort, the incidence of treatment-requiring ROP was 8.2%, which is comparable to the 6.7% incidence of severe ROP previously reported in Türkiye [37].

The incidence of severe IVH is nearly 7-15% in VLBW infants. In the previous Turkish multicenter study, the incidence of severe IVH (>Grade II according to Papile staging) was reported as 5.4% [5]. In the current study,

ARTICLE IN PRESS

the incidences of any and severe IVH were 28% and 8.7%, respectively. In the Swiss study, the incidence of severe IVH was 3.5% in survived VLBW infants and 5.7% in the US-VON study [30]. The incidence of IVH in our study was higher than that reported in developed countries, a difference that may be attributable to the combined effects of the antenatal and postnatal clinical care practice factors discussed above.

According to a recent US multicenter study including 10,877 ELBW infants born at 22-28 weeks' GA between 2013-2018, the incidences of NEC, LOS, severe IVH, severe ROP, and severe BPD were 8.9%, 19.9%, 14.3%, 12.8%, and 8%, respectively [30]. These findings indicate that the incidence of neonatal morbidities in infants ≤28 weeks in the US study is comparable to that observed in infants <32 weeks in our cohort. Therefore, although Türkiye has undertaken substantial efforts to improve perinatal and neonatal outcomes related to prematurity, further improvements in antenatal and postnatal care remain necessary for better neonatal outcomes.

The survival rate of VLBW infants is reported to be over 90% in developed countries. [30,38]. The overall mortality rate of VLBW infants from Latin American countries was 26.8% [39]. In the present study, as 78.2% of VLBW infants survived to discharge, overall mortality was 21.7%. The early neonatal, neonatal, and in-hospital mortality rates were reported as 3.9%, 6.0%, and 7.5%, respectively, in the multicenter study of the eNewborn European Network database [38]. The early, late and post-neonatal mortality

ARTICLE IN PRESS

rates in our study were 12.7%, 6.2% and 2.9%, respectively. Therefore, early neonatal mortality is higher in Türkiye compared with European countries.

The survival rate to discharge for extremely premature infants (between 22 and 28 weeks) was reported to be 78.3% in US [11]. The mortality was found as 34.8% among infants born at ≤28 weeks' GA in our study. Therefore, the survival rate for infants with GA <32 weeks in Türkiye (79%) appears comparable to the survival rate reported for infants <28 weeks in US, while overall remaining intermediate between rates observed in developed and developing countries. All these data show that there is a considerable gap in the survival rates of preterm infants between developing and developed countries. It is reasonable to underscore the need of several improvements from DR to NICU practices to reach the status of developed countries and also to achieve more favorable neonatal outcomes in Türkiye.

Strength and limitations

The strength of the present study was its large, multicenter design that allowed for prospective data collection via a specialized network. In addition, most of the centers represent reference NICUs in which neonatologists work as the primary physicians.

There are some limitations of the study. NICUs with no neonatologists or NICUs including neonatologists who did not agree to participate in the study were not included. This was a limitation, as these might increase the overall rates of mortality and morbidities. Also, the neonatologists did not undertake any training to standardize the definitions of potential risk factors

ARTICLE IN PRESS

before the study. Furthermore, due to the BW-based inclusion criterion (<1500 g), exclusion of infants born at later GA (> 31 weeks) from the study cohort, with the idea of they highly represent a population of growth-restricted infants rather than very preterm infants, may also have introduced selection bias and influenced the interpretation of associations between maternal characteristics and neonatal outcomes. Similarly, exclusion of infants born at 22 weeks of GA with the same purpose may also be considered as a limitation. In addition, the lack of data including DR deaths and the number of infants who could not be admitted to NICUs within the first 24 hours represent another limitation, as these data may provide insights about the evaluation of neonatal resuscitation and transport practices for the country.

Conclusion

In conclusion, the current study provides an important overview for the Turkish population and also other developing countries. Morbidity rate in VLBW infants is a serious concern in Türkiye and higher than those in developed countries. Therefore, strategies to decrease both prematurity-related morbidities and mortality should be developed. Both antenatal and perinatal follow-up programs and care strategies, appropriate DR approaches, and advanced NICU practices should be implemented. In addition, strict follow-up of oxygen therapy with appropriate monitoring, better neonatal care, meticulous attention to hygiene procedures, control of sepsis, promotion of breastfeeding, and training of NICU healthcare

ARTICLE IN PRESS

professionals may also reduce the prevalence of neonatal morbidities. These findings highlight the need for sustained clinical quality improvement efforts, restructuring of perinatal and neonatal care systems, and enhanced antenatal and postnatal care to improve survival free of major prematurity-related morbidities.

Methods

The SECRETS study was promoted by the TNS and was approved by the Local Ethical Committee (Number:2021.03.30). The study was conducted between 28 April 2021 and 02 January 2023 in accordance with the Declaration of Helsinki. A written informed parental consent was obtained from all families. A total of 78 reference level III and IV NICUs from 7 different regions of Türkiye participated. All these NICUs had the expertise to follow up these high-risk premature infants in terms of their medical staff, equipment, and other resources.

ARTICLE IN PRESS

Study population

The inclusion criteria comprised inborn and outborn preterm infants with BW ≤1500 g and GA of $23^{0/7}$ to $31^{6/7}$ weeks who were admitted to the NICU within the first 24 h of life and for whom parental consent was obtained. Preterm infants with GA <32 weeks but BW >1500 g were excluded, as this subgroup represents a distinct clinical population, predominantly consisting of growth-restricted rather than very preterm infants. As the primary objective of the study was to evaluate survival and neonatal outcomes in VLBW infants, whose respiratory physiology, postnatal adaptation, and

ARTICLE IN PRESS

morbidity profiles differ substantially from those of more mature and/or growth-restricted infants, the study cohort was restricted to infants with BW ≤1500 g and GA <32 weeks to ensure a more homogeneous population. In addition, infants born at 22 weeks' gestation were also excluded as resuscitation practices at this threshold vary considerably across centers in Türkiye, largely depending on institutional experience, which may introduce substantial heterogeneity and potential bias for the analysis. Infants who died in the DR, infants admitted to the NICU after the first 24 hours of life, infants with major congenital/chromosomal abnormalities, and those whose parents refused consent were all defined as the exclusion criteria. The maternal, perinatal, and neonatal characteristics, care practices, neonatal morbidities and survival data of all infants were noted.

All data were collected through a web-based data entry system via a special network named 'Trials-Network.' A case report form (CRF) for each included infant was filled out by the neonatologist of the center. All questions in the CRF were compulsory, meaning the data entry system did not allow submission if any question was left unanswered. Database access was password-protected to maintain data security. The records of infants from all 78 NICUs were pooled together and analyzed at the end of the study by the primary investigator.

Clinical data

Both antenatal and perinatal clinical data, including maternal age, parity, administration of antenatal corticosteroids, presence of maternal

ARTICLE IN PRESS

diseases such as preeclampsia, eclampsia, hypertension, and diabetes, multiple births, number of prenatal visit, and mode of delivery were collected. GA was determined using ultrasonography and/or the date of the last menstrual period. Infants were classified as small for gestational age (SGA) and large for gestational age (LGA) if their BW was below the 10th percentile or above the 90th percentile for GA and sex, respectively, according to Fenton growth charts.

The recorded clinical characteristics of infants were as follows: GA, BW, gender, presence of SGA or LGA, multiple births, inborn and outborn status, the need for resuscitation and intubation in the DR, DCC status, the need for surfactant treatment, surfactant administration time, setting and method, the duration of both invasive and non-invasive MV, the duration of hospitalization, medications including probiotics, caffeine and postnatal corticosteroids, duration of TPN, achievement of both full enteral nutrition and also full oral feeding. In-hospital mortality was defined as ‘early neonatal’ (days 1-6), ‘late neonatal’ (days 7-28), and ‘post-neonatal’ (from day 29 to until NICU discharge). For standardized management, all centers were advised to follow the recommendations of the TNS guidelines. The recent NRP recommendations were followed by all centers for the management and resuscitation of inborn infants in the DR [40,41].

In this study, neonatal morbidities comprised RDS, IVH, hsPDA, BPD, NEC, sepsis, and ROP. Notably, RDS was excluded from the composite outcome of survival without major morbidities to avoid statistical bias

ARTICLE IN PRESS

resulting from its high prevalence. IVH (grade ≥3) and/or cystic PVL, NEC (stage ≥2), BPD, ROP (stage ≥3), and neonatal sepsis were defined as major neonatal morbidities affecting survival as previously described [13]. Both survival and survival without major morbidity were calculated using all included infants (n=3042) as the denominator at the final statistical analysis.

RDS was diagnosed if the infant exhibited clinical signs of respiratory distress, required supplemental oxygen and/or assisted ventilation, and had a chest radiograph consistent with RDS. Surfactant was administered according to national and international RDS and surfactant guidelines [42,43]. The presence and severity of IVH were defined according to the Volpe classification and TNS guideline. Cystic PVL was defined as the presence of periventricular cysts identified on cranial ultrasonography or magnetic resonance imaging [44]. The hsPDA requiring medical or surgical treatment was diagnosed as an inner ductal diameter >1.5 mm/kg or >1.4 mm/kg, and/or LA/Ao >1.5, and/or retrograde flow in the descending aorta [45]. Infants who died before echocardiography and/or cranial ultrasonography were not included in the denominators when calculating hsPDA or IVH incidence.

NEC was diagnosed based on clinical and radiographic findings and was classified according to the modified Bell's criteria [46,47]. BPD was defined according to the 2001 National Institute of Child Health and Human Development consensus statement as the requirement for supplemental oxygen for the first 28 days of life and was classified as mild, moderate, or

ARTICLE IN PRESS

severe depending on the duration and level of supplemental oxygen and MV support at 36 weeks postmenstrual age (PMA) [48,49]. The infants who survived to 36 weeks PMA was the denominator for BPD.

ROP was classified according to the International Classification of Retinopathy of Prematurity and TNS ROP guideline screening recommendations were followed [50,51]. ROP was determined among infants who were screened and survived to discharge. Infants who died before first ROP examination were not included to the analysis. Early-onset sepsis was defined as the onset of clinical and laboratory findings at <72 hours of age. LOS was defined as the onset of systemic signs of infection and increased acute-phase reactants at >72 hours of age [52]. LOS was calculated among infants that survived beyond 72 hours of life.

Statistical analysis

The data were analyzed using SPSS Statistics 21.0 software. Demographic variables, care practices, morbidities, and mortality are summarized using descriptive statistics without comparison. Demographic data were presented as number, percentage, mean (±SD), and median (interquartile range (IQR)). The results are displayed by each week of GA. The association between GA categories (≤28 vs >28 weeks) and mortality was evaluated using the Pearson chi-square test. When appropriate, Fisher's exact test was additionally applied to confirm the robustness of the results. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to quantify the strength of association.

ARTICLE IN PRESS

For multivariate analysis, logistic regression models were constructed to identify independent predictors of mortality, NEC, and severe IVH for infants born ≤28 weeks' GA. Variables included in the models were selected based on clinical relevance and statistical significance in univariate analyses ($p < 0.10$). These variables comprised GA, BW, duration of MV within the first 7 days of life, presence of sepsis, exposure to any dose of ACS and sex. Adjusted odds ratios (aORs) with 95% confidence intervals were calculated to determine independent associations. A two-tailed p value of <0.05 was considered statistically significant.

References

1. Bradley, E. et al. Born too soon: global epidemiology of preterm birth and drivers for change. *Reprod Health*. **22(S2),** 105 (2025).
2. Chawanpaiboon, S. et al. Global, regional and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health*. **7(1),** e37-e46 (2019).
3. Ohuma, E.O. et al. National, regional and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. *Lancet*. **402(10409)**, 1261-1271 (2023).
4. Ward, V.C. et al. Overview of the global and US burden of preterm birth. *Clin Perinatol.* **51(2)**, 301-311 (2024).
5. Koc, E, et al. Early neonatal outcomes of very-low-birth weight-infants in Turkey: a prospective multicenter study of the Turkish Neonatal Society. *PLoSOne.* **14(12),** e0226679 (2019).
6. Mowitz, M.E. et al. Burden of comorbidities and healthcare resource utilization among medicaid-enrolled extremely premature infants. *J Health Econ Outcomes Res*. **9,** 147-155 (2022).
7. Atun, R. et al. Universal health coverage in Turkey: enhancement of equity. *Lancet.* **382(9886)**, 65-99 (2013).
8. Demirel, G. et al. Rapid decrease of neonatal mortality in Turkey. *Matern Child Health J.***17:**1215–1221 (2013).
9. Erdeve, O. et al. From national newborn guidelines to international consensus. *Turk Pediatri Ars.* **53(S1):** S1-S2 (2018).

ARTICLE IN PRESS

10. Cao, G., Liu, J. & Liu, M. Global, regional and national incidence and mortality of neonatal preterm birth, 1990-2019. *JAMA Pediatr*. **176(8)**, 787-796 (2022).
11. Bell, E.F. et al. Mortality, in-hospital morbidity, care practices, and 2-year outcomes for extremely preterm infants in the US, 2013-2018. *JAMA.* **327(3),** 248-263 (2022).
12. Ashorn, P. et al. Small vulnerable newborns-big potential for impact. *Lancet.* **401(10389)**, 1692-1706 (2023).
13. Cao, Y. et al. Assesment of neonatal intensive care unit practices, morbidity and mortality among very preterm infants in China. *JAMA Netw Open.* **4(8)**, e2118904 (2021).
14. Sartorius, V. et al. Neonatal mortality disparities by gestational age in European countries. *JAMA Netw Open.* **7(8)**, e2424226 (2024).
15. Horbar, J.D. et al. Trends in mortality and morbidities for infants born 24 to 28 weeks in the US: 1997-2021. *Pediatrics.* **153(1)**, e2023064153 (2024).
16. Edwards, E.M., Ehret, D.E.Y., Soll, R.F. & Horbar, J.D. Survival of infants born at 22 to 25 weeks' gestation receiving care in the NICU: 2020-2022. *Pediatrics.* **154(4)**, e2024065963 (2024).
17. Morgan, A.S. et al. Birth outcomes between 22 and 26 weeks' gestation in national population-based cohorts from Sweden, England and France. *Acta Paediatr.* **111(1):**59-75 (2022).
18. Hofmeyer, G.J. et al. Evidence-based antenatal interventions to reduce the incidence of small vulnerable newborns and their associated poor outcomes. *Lancet.* **401(10389),**1733-1744 (2023).
19. McGoldrick, E., Stewart, F., Parker, R. & Dalziel, S.R. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev.* **12(12)**, CD004454 (2020).
20. Manley, B.J. et al. Intratracheal budesonide mixed with surfactan for extremely preterm infants: the PLUSS randomized clinical trial. *JAMA.* **332(22),**1889-1899 (2024).
21. Hundscheid, T. et al. Expectant management or early ibuprofen for patent ductus arteriosus. *N Engl J Med.* **388(11)**, 980-990 (2023).
22. Watterberg, K.L. et al. Hydrocortisone to improve survival without bronchopulmonary dysplasia. *N Engl J Med.* **386(12)**, 1121-1131 (2022).
23. Chiruvolu, A. et al. Variations in umbilical cord clamping practices in the United States: a national survey of neonatologists*. J Matern Fetal Neonatal Med*. **35(19)**,3646-3652 (2022).

ARTICLE IN PRESS

ARTICLE IN PRESS

24. Payne, L., Walker, K.F. & Mitchell, E.J. Timing of umbilical cord clamping for preterm infants in low-and-middle-income countries: a survey of current practice. *Eur J Obstet Gynecol Reprod Biol.* **264,** 15-20 (2021).
25. Gizzi, C. et al. Variation in delivery room management of preterm infants across Europe: a survey of the Union of European Neonatal and Perinatal Societies. *Eur J Ped.* **182(9),** 4173-4183 (2023)
26. Tana, M. et al. Respiratory management of the preterm infant: supporting evidence-based practice at the bedside. *Children (Basel).* **10(3)**, 535 (2023).
27. Moretti, C. et al. A survey of the Union of European Neonatal and Perinatal Societies on neonatal respiratory care in neonatal intensive care units. *Children (Basel)*. **11(2),**158 (2024).
28. Lapcharoensap, W. et al. Hospital variation and risk factors for bronchopulmonary dysplasia in a population-based cohort. *JAMA Pediatr*.**169**, e1436 (2015).
29. Mehra, K. & Kresch, M. Trends in the incidence of bronchopulmonary dysplasia after the introduction of neurally adjusted ventilatory assist (NAVA). *Children (Basel)*. ***11(1*****),**113 (2024).
30. Adams, M. et al. & Swiss Neonatal Network and the Vermont Oxford Network. Variability of very low birth weight infant outcome and practice in Swiss and US neonatal units. *Pediatrics.* **141(5),** e20173436 (2018).
31. Alur, P. & Ramarao, S. Transition phase of nutrition-optimizing nutrient administration. *Front Pediatr.* **13,** 1658550 (2025).
32. Battersby, C., Santhalingam, T., Costeloe, K. & Modi, N. Incidence of neonatal necrotising enterocolitis in high-income countries: a systematic review. *Arch Dis Child Fetal Neonatal Ed*. **103(2),** F182-F189 (2018).
33. Stoll, B.J. et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics.* **110(2)**, 285-291 (2002).
34. Isayama, T. et al. Patent ductus arteriosus management and outcomes in Japan and Canada: comparison of proactive and selective approaches. *Am J Perinatol*. **32,**1087-1094 (2015).
35. Okulu, E. et al. An observational, prospective, multicenter, registry-based cohort study comparing conservative and medical management for patent ductus arteriosus. *Front Pediatr.* **8**, 434 (2020).
36. Hong, E.H., Shin, Y.U. & Cho, H. Retinopathy of prematurity: a review of epidemiology and current treatment strategies. *Clin Exp Pediatr*. **65(3)**,115-126 (2021).

ARTICLE IN PRESS

ARTICLE IN PRESS

37. Bas, A.Y. et al. Incidence, risk factors and severity of retinopathy of prematurity in Turkey (TR-ROP study): a prospective, multicentre study in 69 neonatal intensive care units. *Br J Ophthalmol.* **102,**1711-1716 (2018).
38. Haumont, D. et al. Evaluating preterm care across Europe using the eNewborn European Network database. *Pediatr Res*. **88(3),** 484-495 (2020).
39. D'Apremont, I. et al. Trends in perinatal practices and neonatal outcomes of very low birth weight infants during a 16-year period at NEOCOSUR centers. *J Pediatr.* **225**, 44-50 (2020).
40. Oygur, N., Onal, E & Zenciroglu, A. National guidelines for delivery room management. *Turk Pediatri Ars*. **53(S1)**, S3-S17 (2018).
41. Aziz, K. et al. Part 5: Neonatal Resuscitation 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Pediatrics.* **147(S1),**e 2020038505e (2021).
42. Sweet, D.G. et al. European consensus guidelines on the management of respiratory distress syndrome-2019 update. *Neomatology*. **115(4)**, 432-450 (2019).
43. Ozkan, H., Erdeve, O. & Kutman, G.K. Turkish Neonatal Society guideline on the management of respiratory distress syndrome and surfactant treatment. *Turk Pediatr Ars.* **53(S1),** S45-54 (2018).
44. Cizmeci, M.N., Akın, M.A. & Ozek, E. Turkish Neonatal Society Guideline on the diagnosis and management of germinal matrix hemorrhage-intraventricular hemorrhage and related complications. *Turk Arch Pediatr*. **56(5)**, 499-512 (2021).
45. Koksal, N., Aygun, C. & Uras, N. Turkish Neonatal Society guideline on the management of patent ductus arteriosus in preterm infants. *Turk Pediatri Ars*. **53(S1),** S76-S87 (2018).
46. Walsh, M.C. & Kliegman, R.M. Necrotizing enterocolitis: treatment based onstaging criteria. *Pediatr Clin North Am.* **33(1)**,179-201 (1986).
47. Ergenekon, E., Tayman, C. & Ozkan, H. Turkish Neonatal Society Necrotizing Enterocolitis Diagnosis, Treatment and Prevention Guidelines. *Turk Arch Pediatr.* **56(5),** 513-524 (2021).
48. Jobe, A.H. & Bancalari, E. Bronchopulmonary dysplasia. *Am J Respir Crit Care Med.* **163(7),** 1723-1729 (2001).
49. Arsan, S., Korkmaz, A. & Oguz, S. Turkish Neonatal Society guideline on prevention and management of bronchopulmonary dysplasia. *Turk Pediatri Ars.* **53(S1**), 38-50 (2018).
50. Chiang, M.F. et al. International Classification of Retinopathy of Prematurity, Third Edition. *Ophthalmology*. **128(10),** e51-e68 (2021).

ARTICLE IN PRESS

ARTICLE IN PRESS

51. Koc, E., Bas, A.Y., Ozdek, S., Ovalı, F. & Basmak, H. Turkish Neonatal and Turkish Ophtalmology Societies consensus guideline on the retinopathy of prematurity. *Turk Pediatri Ars.* **53 (S1),** S151-S160 (2018).
52. Satar, M., Arısoy, A.E. & Celik, I.H. Turkish Neonatal Society guideline on neonatal infections-diagnosis and treatment. *Turk Pediatri Ars*. **53(S1),** S88-S100 (2018).

Turkish Neonatal Society SECRETS Study Group

Kavurt S[5], Okur NM[6], Buyukeren M[7], Ozcan B[7], Varal IG[8], Dogan P[8], Karabay M[9], Koksal N[10], Ozkan H[10], Armangil D[11], Tayman C[12], Dizdar EA[12], Akar S[13], Mert MK[14], Cekinmez E[14], Oygur N[15], Ongun H[15], Yıldızdas HY[16], Ozlu F[16], Torer B[17], Cetinkaya B[17], Demirel G[18], Gundogdu S[18], Okulu E[19], Kostekci YE[19], Bulut E[20], Arslanoglu S[20], Tekgunduz KS[21], Kara M[21], Duman N[22], Erdogan FT[22], Orman A[23], Celik Y[23], Altunhan H[24], Karaarslan F[24], Kahveci H[25], Yurttutan S[26], Konak M[27], Uygun SS[27], Ozek E[28], Gucyetmez ZST[28], Saglam O[29], Taskın E[30], Benli S[30], Calkavur S[31], Kalkanlı OH[31], Dorum BA[32], Arslan S[32], Beken S[33], Toygar AK[33], Ozdemir O[34], Demir GS[34], Terek D[35], Orel B[35], Akın MA[36], Takçı S[36], Uslu HS[37], Unal ET[37], Gursoy T[38], Hamilcıkan S[39], Can E[39], Tanrıverdi S[40], Abbasoglu A[41], Kefeli M[41], Ciftdemir NA[42], Onal E[3], Karagol BS[43], Calısıcı E[43], Ozdemir R[44], Alagoz M[44], Yılmaz FH[45], Yumlu K[45], Olukman O[46], Ayar M[46], Narter F[47], Topçu B[47], Say BL[48], Kaya TB[49], Tutal M[49], Er I[50], Dönmez T[50], Kanburoglu MK[51],Altıntas O[51], Akın IM[52], Atay FY[52], Ergor SN[53], Ecevit A[54], Aksu M[54], Tüfekçi S[55], Arcagok BC[56], Aydogan S[57], Zenciroğlu A[57], Bilgin L[58], Sandal G[59], Cetin H[59], Ertugrul S[60], Deger I[60], Mutlu M[61], Kader S[61], Yılmaz A[62], Vural M[62], Arman D[63], Kara N[63], Gunlemez A[64], Gurpınar R[64], Kalyoncu O[65], Colak R[66], Celik FC[67], Demir N[68], Akcan

ARTICLE IN PRESS

AB[69], Anık A[69], Cakir SC[70], Buyuktiryaki M[71], Kılıcbay F[72], Tunc G[72], Ercan TE[73], Bastug O[74], Ozdemir A[74],Oguz D[75], Celik HT[76], İyigun I[76], Tuncer O[77], Sonmez B[77], Dilek M[78], Tas S[78], Sahin S[79], Oncel MY[79], Kahvecioglu D[80], Cetinkaya AK[80]

Affiliations

[5] Division of Neonatology, Department of Pediatrics, Health Sciences University, Etlik Zubeyde Hanim Women's Training and Research Hospital, Ankara, Türkiye

[6] Division of Neonatology, Department of Pediatrics, Diyarbakır Gazi Yasargil Training and Research Hospital, Diyarbakır, Türkiye

[7] Division of Neonatology, Department of Pediatrics, Health Sciences University, Konya City Hospital, Konya, Türkiye

[8] Division of Neonatology, Department of Pediatrics, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Türkiye

[9] Division of Neonatology, Department of Pediatrics, Sakarya University, Faculty of Medicine, Sakarya, Türkiye

[10] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Bursa Uludag University, Bursa, Türkiye

[11] Division of Neonatology, Department of Pediatrics, Ankara Koru Hospital, Ankara, Türkiye

[12] Division of Neonatology, Department of Pediatrics, Health Sciences University, Ankara Bilkent City Hospital, Ankara, Türkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[13]Division of Neonatology, Department of Pediatrics, Adıyaman University, Faculty of Medicine, Adıyaman, Türkiye

[14] Division of Neonatology, Department of Pediatrics, Adana City Hospital, Adana, Türkiye

[15]Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Akdeniz University, Antalya, Türkiye

[16] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Cukurova University, Adana, Türkiye

[17] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Baskent University Adana Training and Research Hospital, Adana, Türkiye

[18] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Medipol University, Istanbul, Türkiye

[19] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Ankara University, Ankara, Türkiye

[20] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Medeniyet University, Goztepe Professor Suleyman Yalcın City Hospital, Istanbul, Türkiye

[21] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Ataturk University, Erzurum, Türkiye

[22] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Dokuz Eylul University, Izmir, Türkiye

[23] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Mersin University, Mersin, Türkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[24] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Necmettin Erbakan University, Konya, Türkiye

[25]Division of Neonatology, Department of Pediatrics, Erzurum Training and Research Hospital, Erzurum, Türkiye

[26] Division of Neonatology, Department of Pediatrics, Kahramanmaras Sutcu Imam University, Kahramanmaras, Türkiye

[27] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Selcuk University, Konya, Türkiye

[28]Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Marmara University, Pendik Training and Research Hospital, Istanbul, Türkiye

[29] Division of Neonatology, Department of Pediatrics, Gaziantep Cengiz Gokcek Obstetrics and Children Hospital, Gaziantep, Türkiye

[30]Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Fırat University, Elazıg, Türkiye

[31] Division of Neonatology, Department of Pediatrics, Health Sciences University, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, Izmir, Türkiye

[32] Division of Neonatology, Department of Pediatrics, Bursa City Hospital, Bursa, Türkiye

[33] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Acıbadem Mehmet Ali Aydınlar University, Atakent Hospital, Istanbul, Türkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[34] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Pamukkale University, Denizli, Türkiye

[35] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Ege University, Izmir, Türkiye

[36] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Ondokuz Mayıs, Samsun, Türkiye

[37] Division of Neonatology, Department of Pediatrics, Health Sciences University, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Türkiye

[38] Division of Neonatology, Department of Pediatrics, Koc University, Istanbul, Türkiye

[39] Division of Neonatology, Department of Pediatrics, Health Sciences University, Bagcılar Training and Research Hospital, Istanbul, Türkiye

[40] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Celal Bayar University, Manisa, Türkiye

[41] Division of Neonatology, Department of Pediatrics, Tepecik Training and Research Hospital, Izmir, Türkiye

[42] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Trakya University, Edirne, Türkiye

[43] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Gulhane University, Ankara, Türkiye

[44] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Inonu University, Malatya, Türkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[45] Division of Neonatology, Department of Pediatrics, Konya Ali Kemal Behrivanlı Obstetrics and Children Hospital, Konya, Türkiye

[46] Division of Neonatology, Department of Pediatrics, Bakırcay University, Izmir, Türkiye

[47] Division of Neonatology, Department of Pediatrics, Health Sciences University, Kartal Training and Research Hospital, Istanbul, Türkiye

[48] Division of Neonatology, Department of Pediatrics, Gebze Medical Park Hospital, Kocaeli, Türkiye

[49] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Eskisehir Osmangazi University, Eskisehir, Türkiye

[50] Division of Neonatology, Department of Pediatrics, Kocaeli Derince Training and Research Hospital, Kocaeli, Türkiye

[51] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Recep Tayyip Erdogan University, Rize, Türkiye

[52] Division of Neonatology, Department of Pediatrics, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Türkiye

[53] Division of Neonatology, Department of Pediatrics, Bezmi Alem University, Faculty of Medicine, Istanbul, Türkiye

[54] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Baskent University, Ankara, Türkiye

[55] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Namık Kemal University, Tekirdag, Türkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[56] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Acıbadem Mehmet Ali Aydınlar University, Altunizade Hospital, Istanbul, Türkiye

[57] Division of Neonatology, Department of Pediatrics, Health Sciences University, Dr Sami Ulus Maternity and Children's Hospital, Ankara, Türkiye

[58] Division of Neonatology, Department of Pediatrics, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Türkiye

[98] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Suleyman Demirel University, Isparta, Türkiye

[60] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Dicle University, Diyarbakır, Türkiye

[61] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Karadeniz Teknik University, Trabzon, Türkiye

[62] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Istanbul Cerrahpasa University, Istanbul, Türkiye

[63] Division of Neonatology, Department of Pediatrics, Health Sciences University, Istanbul Training and Research Hospital, Istanbul, Turkiye

[64] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Kocaeli University, Kocaeli, Turkiye

[65] Division of Neonatology, Medicine Hospital, Istanbul, Turkiye

[66] Division of Neonatology, Department of Pediatrics, Altınbas University, Istanbul, Turkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[67] Division of Neonatology, Department of Pediatrics, Baskent University, Istanbul, Turkiye

[68] Division of Neonatology, Esencan Hospital, Istanbul, Turkiye

[69] Division of Neonatology, Department of Pediatrics, Adnan Menderes University, Aydın, Turkiye

[70] Division of Neonatology, Department of Pediatrics, Samsun Training and Research Hospital, Samsun, Turkiye

[71] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Medipol University Nisa Hospital, Istanbul, Turkiye

[72] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkiye

[73] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Maltepe University, Istanbul, Turkiye

[74] Division of Neonatology, Department of Pediatrics, Kayseri City Hospital, Kayseri, Turkiye

[75] Division of Neonatology, Department of Pediatrics, Haseki Training and Research Hospital, Istanbul, Turkiye

[76] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkiye

[77] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Yuzuncu Yıl University, Van, Turkiye

[78] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Abant İzzet Baysal University, Bolu, Turkiye

ARTICLE IN PRESS

ARTICLE IN PRESS

[79] Division of Neonatology, Department of Pediatrics, Buca Seyfi Demirsoy Training and Research Hospital, Izmir, Turkiye

[80] Division of Neonatology, Department of Pediatrics, Ankara Training and Research Hospital, Ankara, Turkiye

Statements

Author Contributions

Study concept and design: M.C, S.M, E.K, and A.B.Y. Acquisition, analysis and interpretation of the data: M.C, S.M, and A.B.Y Drafting the manuscript: M.C, S.M, E.K, and A.B.Y**. Statistical analysis:** M.C, S.M, and A.B.Y**. Writing - original draft, Writing - review & editing**: M.C, E.K, and A.B.Y. All authors reviewed the manuscript.

Data availability statement: The data that support the findings of this study are available on request from the corresponding author, MC. The data are not publicly available due to ethical considerations that could compromise the privacy of research participants.

Funding Statement: This study was supported by Turkish Neonatal Society for the establishment of the web-based data entry system (Trials-Network) and formation of the study case report form (CRF). The funding organization had no role in the study design, data collection and analysis, preparation of the manuscript.

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

ARTICLE IN PRESS

ARTICLE IN PRESS

Trial registration: Clinical trials gov**,** Survival and Neonatal Outcomes of Very Low Birth Weight Infants in Türkiye: Turkish Neonatal Society SECRETS-TR Study (TNS-SECRETS), NCT 06543524, 2024-08-07

Ethical Approval: This study was approved by the Basaksehir Cam Sakura City Hospital Ethics Committee (protocol number:2021.03.30), and was conducted in accordance with the Declaration of Helsinki.

Figure Legends

Figure 1. Survival with or without major morbidity of very preterm infants (<32 weeks' gestation).

Tables Legends

Table 1. Neonatal and maternal characteristics of the study group

Table 2. Delivery room and NICU practices of the study group

Table 3. Incidences of prematurity-related neonatal morbidities

Table 4. Survival without major morbidity and mortality rates

Table 5. Multivariate logistic regression analysis for mortality, NEC, and severe IVH in infants ≤28 weeks of gestational age

ARTICLE IN PRESS

Table 1. Neonatal and maternal characteristics of the study group

Gestational week	Total	23 n (%)	24 n (%)	25 n (%)	26 n (%)	27 n (%)	28 n (%
Neonatal characteristics							
Number of infants	3042	104	193	230	325	381	44
Gestational age, Mean (SD), weeks	27(2.2)	23.7(0.4)	24.3(0.3)	25.4(0.3)	26.4(0.4)	27.5(0.4)	28.4(
Birth weight, Median (range), gram	1080(320-1500)	570(320-850)	640(520-950)	760(600-1060)	870(600-1280)	970(620-1320)	1100(138
Sex, male(%)	1464(48)	52(50)	98(51)	122(53)	175(54)	172(45)	221(
AGA, n(%) **SGA, n(%)** **LGA, n(%)**	2629(86) 328(11) 85(3)	86(83) 13(12) 5(4)	162(84) 25(13) 6(3)	194(84) 21(9) 15(6)	292(90) 19(6) 14(4)	317(83) 45(12) 19(5)	385(44(1 17(
Multiple birth, n (%)	743(24)	18(17)	43(22)	63(27)	77(24)	84(22)	90(2
Outborn status	97(3.2)	4(3.8)	6(3.1)	7(3)	8(2.4)	6(1.6)	17(3

ARTICLE IN PRESS

Maternal characteristics							
Age, mean (SD), y	29.2(5)	29.7(6.3)	28.3(6.2)	29.3(5.5)	29(6.2)	29.6(5.6)	29.3(
Cesarean delivery	2650(87.1)	70(67.3)	149(77.2)	194(84.3)	284(87.3)	342(89.7)	387(8
Antenatal corticosteroid therapy	2207 (72.5)	55(52.8)	125(64.7)	158(68.6)	232(71.3)	288(75.5)	316(7
Primigravida	1442(47)	45(43)	94(48)	101(44)	165(51)	164(43)	201(
Maternal diseases	1155(38)	28(27)	57(29)	79(34)	106(33)	151(40)	178(
Diabetes	183(6)	1(1)	6(3)	10(4)	7(2)	35(9)	21(
Hypertension	588(19)	9(8)	23(12)	27(12)	50(15)	74(19)	78(1
Preeclampsia	516(17	7(6)	19(10)	25(11)	45(14)	71(18)	64(1
Eclampsia	26(0.8)	1(1)	1(0.4)	1(0.4)	2(0.6)	3(0.8)	6(1.
≥1 Prenatal visit	2258(74)	67(64)	126(65)	164(71)	254(78)	294(77)	313(

Abbreviations: AGA, appropriate for gestational age; LGA,large for gestational age; SD, standart deviation; SGA, small for gestational age

Table 2. Delivery room and NICU practices of the study group

Characteristics -Gestational week	Total n (%)	23 n (%)	24 n (%)	25 n (%)	26 n (%)	27 n (%)	28 n (%)
Number	3042	104	193	230	325	381	446
Delivery room resuscitation							
Pozitive pressure ventilation	1823(59.9)	101(97.1)	174(90)	190(82.6)	233(71.6)	257(67.4)	273(61.
Intubation	1177(38.6)	95(91.3)	151(78)	159(69.1)	175(53.8)	144(37.7)	177(39.
Chest compression	99(3.2)	15(14.4)	20(10)	10(4.3)	10(3)	12(3.1)	14(3.1
Epinephrine	40(1.3)	3(2.8)	12(6)	1(0.4)	3(0.9)	5(1.3)	7(1.5)
Delayed cord clamping for 30 s	401(13.1)	6(5.7)	12(6)	25(10.8)	29(8.9)	48(12.5)	68(15.2
Delayed cord clamping for 60 s	255(8.3)	-	5(3)	14(6)	18(5.5)	49(12.8)	43(9.6
Surfactant therapy							
DR	188(6.2)	12(11.5)	14(7.3)	31(13.5)	27(8.3)	22(5.8)	34(7.6
NICU	1573(51.7)	55(52.9)	122(63.2)	134(58.3)	193(59.4)	238(62.5)	256(57.
DR+NICU	350(11.5)	34(32.7)	54(28)	45(19.6)	53(16.3)	43(11.3)	57(12.8
LISA	244(8)	1(1)	6(3.1)	7(3)	25(7.7)	45(11.8)	39(8.7
MIST	52(1.7)	-	-	5(2.2)	3(0.9)	9(2.4)	8(1.8)
Postnatal corticosteroids							
Systemic	687(22.5)	17(16.3)	57(29.5)	72(31.3)	118(36.3)	118(30.9)	129(28.
İnhaled	360(11.8)	9(8.6)	30(15.5)	35(15.2)	67(20.6)	66(17.3)	64(14.3
Non-invasive ventilation	1497 (49.2)	7(6.7)	29(15)	46(20)	101(31)	182(47.7)	215(48.
Conventional invasive ventilation	1492(49)	97(93.2)	164(84.9)	184(80)	221(68)	196(51.4)	227(50.
High frequency ventilation	57(1.8)	6(5.7)	9(4.6)	7(3)	14(4.3)	10(2.6)	3(1)
Duration of invasive mechanical ventilation							
In the first 7 days, hours (median [IQR])	150(140-160)	160(155-165)	160(155-165)	150(145-155)	145(140-150)	150(140-160)	150(14 160)
In survivors	120(100-135)	76(66-86)	96(90-100)	144(135-150)	100(90-110)	118(110-125)	124(11 132)
In non-survivors							
Total parenteral nutrition (TPN), n(%)	2930(96.3)	103(99)	187(96.9)	224(97.3)	323(99.4)	367(96.3)	437(98
Duration of TPN, days,median(IQR)	12(8-16)	6(4-8)	14(11-18)	16(12-18)	14(10-19)	14(11-18)	13(9-16

ARTICLE IN PRESS

ARTICLE IN PRESS

Administration of oropharingeal mothers milk **none** **< 72 h** **≥ 72 h**	2254(74) 744(24.5) 44(1.4)	79(76) 21(20.2) 4(3.8)	136(70.5) 54(28) 3(1.5)	176(76.5) 48(20.9) 6(2.6)	233(71.7) 87(26.8) 5(1.5)	272(71.4) 105(27.6) 4(1)	329(73. 111(24. 6(1.3)
Minimal enteral nutrition **none** **< 24 h** **≥ 24 h**	563(18.5) 1348(44.3) 1131(37.1)	53(51) 19(18.2) 32(30.8)	60(31) 54(28) 79(41)	65(28.2) 68(29.6) 97(42)	69(21.2) 138(42.5) 118(36.3)	70(18.3) 171(44.9) 140(36.6)	61(13. 198(44. 187(41.
Full enteral nutrition, days median (IQR)	19(15-24)	122(110-135)	104(90-120)	62(54-70)	30(20-38)	22(15-29)	18(14-2
Full oral feeding, days median(IQR)	49(40-59)	155(140-170)	140(125-158)	112(99-125)	83(70-95)	61(50-75)	50(40-6
Probiotics	326(10.7)	4(3.8)	13(6.7)	16(6.9)	38(11.6)	56(14.6)	44(9.8
Caffein	2709(89)	96(92.3)	184(95.3)	221(96)	321(98.7)	365(95.8)	426(95.
Duration of caffeine, days median(IQR)	36(30-42)	28(24-32)	37(30-42)	43(35-50)	45(40-50)	46(42-52)	39(32-4
Duration of hospitalization, days median(IQR) **Duration of hospitalization in survivors** **Duration of hospitalization in non-survivors**	56(40-73) 18(8-28)	133(110-150) 12 (6-20)	114(98-135) 19(10-30)	100(80-120) 17(9-26)	80(65-96) 23(12-35)	70(60-82) 22(10-36)	61(50-7 16(9-25

Abbreviations: DR, delivery room; IQR, Interquartile Range; LISA, less invasive surfactant administration; MIST, minimal invasive surfactant therapy; NICU, neonatal intensive care unit

Table 3. Incidences of prematurity-related neonatal morbidities

Gestational week	Total n(%)	23 n(%)	24 n(%)	25 n(%)	26 n(%)	27 n(%)	28 n(%)	
Number of infants	3042 (100)	104 (3.4)	193 (6.3)	230 (7.6)	325 (10.6)	381 (12.5)	446 (14.6)	
RDS	2324(76.3)	104(100)	187(96.8)	213(92.6)	292(89.8)	327(85.8)	378(84.7)	33
BPD **Death before BPD diagnosis** **None** **Diagnosis** **Mild** **Moderate** **Severe**	633(20.8) 1207(39.6) 1202 (39.5) 524(17.2) 231(7.6) 447 (14.7)	83(79.8) 1(0.9) 20 (19.2) 3(2.8) 4(3.8) 13(12.5)	121(62.6) 1(0.5) 71 (36.7) 17(8.8) 16(8.2) 38(19.6)	104(45.2) 7(3) 119 (51.7) 44(19.1) 25(10.8) 50(21.7)	102(31.3) 37(11.3) 186(57.2) 87(26.7) 33(10.1) 66(20.3)	75(19.7) 86(22.6) 220(57.7) 116(30.4) 36(9.4) 68(17.8)	79(17.7) 143(32) 224(50.2) 108(24.2) 51(11.4) 65(14.6)	26 16 8 5
NEC **Death before NEC diagnosis** **None** **Diagnosis** **Stage I** **Stage II** **Stage III**	28 (0.9) 2586(85) 428(14) 177(5.8) 155(5) 96(3.1)	5(4.8) 89(80.7) 15(14.4) 2(1.9) 3(2.8) 10(9.6)	6 (3.1) 145(75) 42(21.7) 11(5.7) 18(9.3) 13(6.7)	4 (1.7) 181(78.7) 45(19.5) 15(6.3) 12(5.2) 18(8)	4(1.2) 262(80) 59(18.1) 19(5.9) 24(7.4) 16(4.9)	2 (0.5) 318(83.5) 61(16) 28(7.3) 22(5.6) 11(2.8)	2 (0.4) 378(84.8) 66(14.8) 30(6.7) 22(4.9) 14(3.1)	4 5

ARTICLE IN PRESS

ROP	**Death before ROP examination**	102(3.3)	10(9.6)	24(12.4)	15(6.5)	15(46.1)	18(4.7)	10(2.2)
	None	2177(71.5)	74(71.1)	107(55.4)	123(53.5)	199(61.2)	218(57.2)	319(71.5)
	Diagnosis	763(25)	20(19.3)	)	92(40)	111(34.7)	145(38.1)	117(26.3)
Anti-VEGF treatment		148(4.8)	9(8.7)	62(32.1)	35(15.2)	23(7.1)	16(4.2)	11(2.5)
Laser photocoagulation		97(3.2)	8(7.7)	32(16.6)	11(4.8)	16(4.9)	23(6)	15(3.4)
Surgical treatment of ROP		6(0.2)	1(1)	9(4.7)	1(0.4)	-	1(0.3)	1(0.2)
				2(1)				
hsPDA	**Death before ECHO**	166(5.4)	36(34.6)	38(19.7)	28(12.1)	20(6.2)	20(5.2)	10(2.2)
	None	1920(63.1)	21(20.2)	55(28.5)	78(33.9)	150(46.2)	214(56.1)	282(63.2)
	Diagnosis	956(31.5)	47(45.2)	100(51.8)	124(54)	155(47.6)	147(38.7)	154(34.6)
				)				
Sepsis	**Sepsis episodes**	1695(55.7)	59(56.7)	126(65.3)	160(69.5)	220(67.7)	257(6.7)	255(57.1)
	Early neonatal sepsis	589(19.3)	25(24)	)	64(27.8)	71(21.8)	85(22.3)	76(17)
	Late neonatal sepsis	1357(44.6)	39(37.5)	54(28)	124(53.7)	186(57.2)	214(56.2)	213(47.9)
				92(47.7)				
IVH	**None**	2192(72)	53(51)	92(47.7)	128(55.7)	191(58.8)	262(68.8)	328(73.5)
	Stage I	360(11.8)	8(7.7)	33(17)	34(14.8)	45(13.8)	46(12)	55(12.3)
	Stage II	194(6.3)	13(12.5)	24(12.4)	17(7.4)	37(11.4)	32(8.4)	27(6)
	Stage III	142(4.6)	13(12.5)	26(13.5)	27(11.7)	25(7.7)	20(5.2)	17(3.8)
	Stage IV	125(4.1)	17(16.3)	14(7.3)	22(9.6)	24(7.4)	19(4.9)	12(2.7)
PVL		29(0,9)	-	4(2)	2(0.9)	3(0.9)	2(0.5)	7(1.6)

Abbreviations: BPD, bronchopulmonary dysplasia; ECHO, echocardiography, hsPDA, hemodynamic significant patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity; VEGF, Vascular endothelial growth factor

ARTICLE IN PRESS

Table 4. Survival without major morbidity and mortality rates

Gestational week	Total n(%)	23 n(%)	24 n(%)	25 n(%)	26 n(%)	27 n(%)	28 n(%)
Number of infants	3042	104	193	230	325	381	446
Survival	2381(78.2)	19(18.2)	66(34.2)	123(53.5)	218(67.1)	303(79.5)	365(81.8)
Survival without major morbidity	1301(42.8)	-	13(7.1)	28(12.4)	72(22.3)	133(35.4)	183(41.2)
Major morbidities affecting survival	296(9.7)	30(2.9)	44(22.8)	51(22.1)	52(16)	41(10.7)	36(8)
IVH ≥ grade 3 or cystic PVL	1202(39.5)	20(19.2)	61(31.6)	119(51.7)	186(57.2)	220(57.7)	224(50.2)
BPD	251(8.3)	13(12.5)	31(16)	30(13)	33(8.6)	36(8)	
NEC ≥ stage 2	1695(55.7)	59(56.7)	126(65.3)	160(69.5)	40(12.3)	257(6.7)	255(57.1)
Sepsis	251(8.3)	18(17.3)	43(22.2)	47(20.4)	220(67.7)	40(10.5)	27(6)
ROP ≥ stage 3					39(12)		

ARTICLE IN PRESS

Mortality	661 (21.7)	85(81.7)	127(65.8)	107(46.5)	107(32.9)	78(20.5)	81(18.2)
Early mortality (1-6 days)	386 (12.7)	53(50.9)	80(41.4)	60(26)	63(19.3)	48(12.5)	41(9.1)
Late mortality (7-28 days)	188(6.2)	26(25)	28(14.5)	33(14.3)	26(8)	22(5.8)	30(6.7)
Post-neonatal mortality (day 29 to until discharge)	87(2.9)	6(5.8)	19(9.8)	14(6)	18(5.5)	8(2.1)	10(2.2)

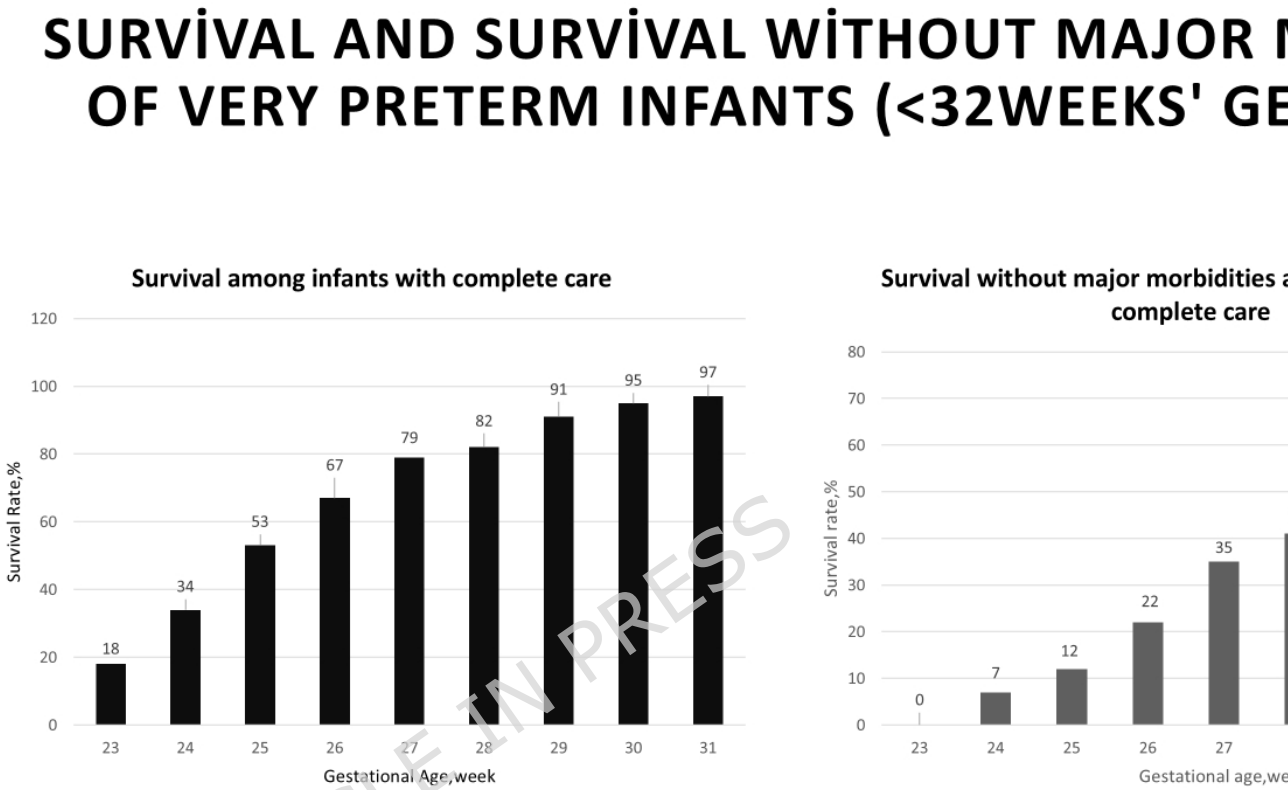
Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.

Table 5. Multivariate logistic regression analysis for mortality, NEC, and severe IVH in infants ≤28 weeks of gestational age

	Mortality (aOR, 95% CI)	**p-value**	**NEC (aOR, 95% CI)**	**p-value**	**Severe IVH (aOR CI)**
(per 1-week decrease)	1.45 (1.30–1.62)	**<0.001**	1.20 (1.08–1.34)	**0.001**	1.32 (1.18–1.4
er 100 g decrease)	1.28 (1.18–1.39)	**<0.001**	1.15 (1.05–1.26)	**0.003**	1.22 (1.12–1.3
tilation (first 7 days, per	1.12 (1.06–1.18)	**<0.001**	1.08 (1.03–1.14)	**0.002**	1.10 (1.05–1.1
s	2.10 (1.65–2.68)	**<0.001**	1.85 (1.42–2.41)	**<0.001**	1.40 (1.10–1.7
ids (any use)	0.68 (0.54–0.85)	**0.001**	0.75 (0.60–0.95)	**0.02**	0.70 (0.55–0.8
	1.22 (0.98–1.52)	0.07	1.10 (0.88–1.38)	0.40	1.18 (0.95–1.4

Abbreviations: IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis

ARTICLE IN PRESS

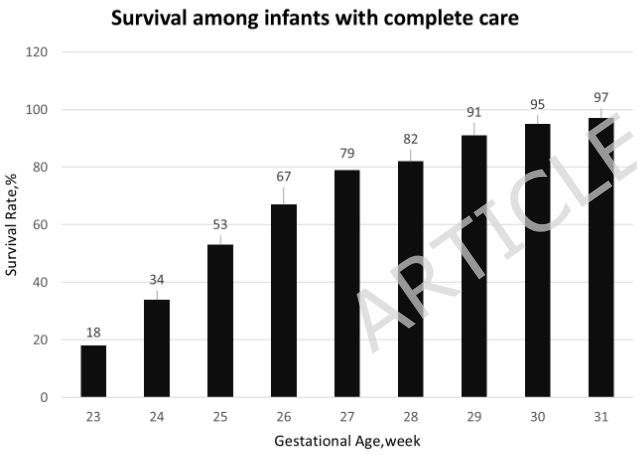


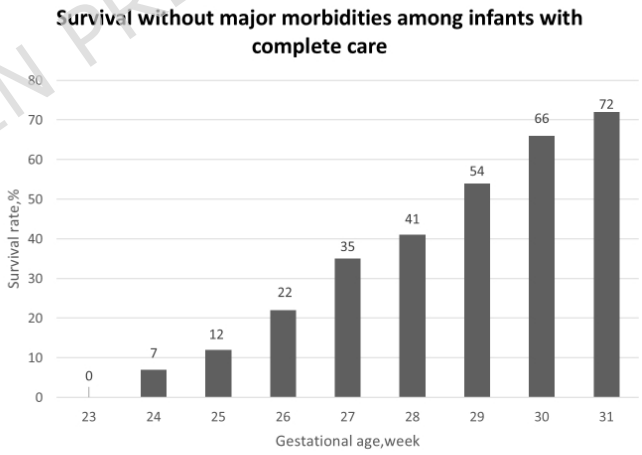
ARTICLE IN PRESS

Figure 1. Survival with or without major morbidity of very preterm infants (<32 weeks' gestation).

ARTICLE IN PRESS

SURVİVAL AND SURVİVAL WİTHOUT MAJOR MORBİDİTY OF VERY PRETERM INFANTS (<32WEEKS' GESTATİON)





ARTICLE IN PRESS

ARTICLE IN PRESS

Table 1. Neonatal and maternal characteristics of the study group

Gestational week	Total	23 n (%)	24 n (%)	25 n (%)	26 n (%)	27 n (%)	28 n (%
Neonatal characteristics							
Number of infants	3042	104	193	230	325	381	44
Gestational age, Mean (SD), weeks	27(2.2)	23.7(0.4)	24.3(0.3)	25.4(0.3)	26.4(0.4)	27.5(0.4)	28.4(
Birth weight, Median (range), gram	1080(320-1500)	570(320-850)	640(520-950)	760(600-1060)	870(600-1280)	970(620-1320)	1100(138
Sex, male(%)	1464(48)	52(50)	98(51)	122(53)	175(54)	172(45)	221(
AGA, n(%) **SGA, n(%)** **LGA, n(%)**	2629(86) 328(11) 85(3)	86(83) 13(12) 5(4)	162(84) 25(13) 6(3)	194(84) 21(9) 15(6)	292(90) 19(6) 14(4)	317(83) 45(12) 19(5)	385(44(1 17(
Multiple birth, n (%)	743(24)	18(17)	43(22)	63(27)	77(24)	84(22)	90(2
Outborn status	97(3.2)	4(3.8)	6(3.1)	7(3)	8(2.4)	6(1.6)	17(3
Maternal characteristics							
Age, mean (SD), y	29.2(5)	29.7(6.3)	28.3(6.2)	29.3(5.5)	29(6.2)	29.6(5.6)	29.3(
Cesarean delivery	2650(87.1)	70(67.3)	149(77.2)	194(84.3)	284(87.3)	342(89.7)	387(8
Antenatal corticosteroid therapy	2207 (72.5)	55(52.8)	125(64.7)	158(68.6)	232(71.3)	288(75.5)	316(7
Primigravida	1442(47)	45(43)	94(48)	101(44)	165(51)	164(43)	201(
Maternal diseases	1155(38)	28(27)	57(29)	79(34)	106(33)	151(40)	178(
Diabetes	183(6)	1(1)	6(3)	10(4)	7(2)	35(9)	21(
Hypertension	588(19)	9(8)	23(12)	27(12)	50(15)	74(19)	78(1
Preeclampsia	516(17	7(6)	19(10)	25(11)	45(14)	71(18)	64(1
Eclampsia	26(0.8)	1(1)	1(0.4)	1(0.4)	2(0.6)	3(0.8)	6(1.
≥1 Prenatal visit	2258(74)	67(64)	126(65)	164(71)	254(78)	294(77)	313(

ARTICLE IN PRESS

Abbreviations: AGA, appropriate for gestational age; LGA,large for gestational age; SD, standart deviation; SGA, small for gestational age

Table 2. Delivery room and NICU practices of the study group

Characteristics -Gestational week	Total n (%)	23 n (%)	24 n (%)	25 n (%)	26 n (%)	27 n (%)	28 n (%)
Number	3042	104	193	230	325	381	446
Delivery room resuscitation **Pozitive pressure ventilation** **Intubation** **Chest compression** **Epinephrine** **Delayed cord clamping for 30 s** **Delayed cord clamping for 60 s**	 1823(59.9) 1177(38.6) 99(3.2) 40(1.3) 401(13.1) 255(8.3)	 101(97.1) 95(91.3) 15(14.4) 3(2.8) 6(5.7) -	 174(90) 151(78) 20(10) 12(6) 12(6) 5(3)	 190(82.6) 159(69.1) 10(4.3) 1(0.4) 25(10.8) 14(6)	 233(71.6) 175(53.8) 10(3) 3(0.9) 29(8.9) 18(5.5)	 257(67.4) 144(37.7) 12(3.1) 5(1.3) 48(12.5) 49(12.8)	 273(61. 177(39. 14(3.1 7(1.5) 68(15.2 43(9.6

ARTICLE IN PRESS

Surfactant therapy **DR** **NICU** **DR+NICU**	 188(6.2) 1573(51.7) 350(11.5)	 12(11.5) 55(52.9) 34(32.7)	 14(7.3) 122(63.2) 54(28)	 31(13.5) 134(58.3) 45(19.6)	 27(8.3) 193(59.4) 53(16.3)	 22(5.8) 238(62.5) 43(11.3)	 34(7.6 256(57. 57(12.8
LISA	244(8)	1(1)	6(3.1)	7(3)	25(7.7)	45(11.8)	39(8.7
MIST	52(1.7)	-	-	5(2.2)	3(0.9)	9(2.4)	8(1.8)
Postnatal corticosteroids **Systemic** **İnhaled**	 687(22.5) 360(11.8)	 17(16.3) 9(8.6)	 57(29.5) 30(15.5)	 72(31.3) 35(15.2)	 118(36.3) 67(20.6)	 118(30.9) 66(17.3)	 129(28. 64(14.3
Non-invasive ventilation	1497 (49.2)	7(6.7)	29(15)	46(20)	101(31)	182(47.7)	215(48.
Conventional invasive ventilation **High frequency ventilation**	1492(49) 57(1.8)	97(93.2) 6(5.7)	164(84.9) 9(4.6)	184(80) 7(3)	221(68) 14(4.3)	196(51.4) 10(2.6)	227(50. 3(1)
Duration of invasive mechanical ventilation **In the first 7 days, hours (median [IQR])** **In survivors** **In non-survivors**	 150(140-160) 120(100-135)	 160(155-165) 76(66-86)	 160(155-165) 96(90-100)	 150(145-155) 144(135-150)	 145(140-150) 100(90-110)	 150(140-160) 118(110-125)	 150(14 160) 124(11 132)
Total parenteral nutrition (TPN), n(%)	2930(96.3)	103(99)	187(96.9)	224(97.3)	323(99.4)	367(96.3)	437(98
Duration of TPN, days,median(IQR)	12(8-16)	6(4-8)	14(11-18)	16(12-18)	14(10-19)	14(11-18)	13(9-1
Administration of oropharingeal mothers milk **none** **< 72 h** **≥ 72 h**	 2254(74) 744(24.5) 44(1.4)	 79(76) 21(20.2) 4(3.8)	 136(70.5) 54(28) 3(1.5)	 176(76.5) 48(20.9) 6(2.6)	 233(71.7) 87(26.8) 5(1.5)	 272(71.4) 105(27.6) 4(1)	 329(73. 111(24. 6(1.3)
Minimal enteral nutrition **none** **< 24 h** **≥ 24 h**	 563(18.5) 1348(44.3) 1131(37.1)	 53(51) 19(18.2) 32(30.8)	 60(31) 54(28) 79(41)	 65(28.2) 68(29.6) 97(42)	 69(21.2) 138(42.5) 118(36.3)	 70(18.3) 171(44.9) 140(36.6)	 61(13. 198(44. 187(41.
Full enteral nutrition, days median (IQR)	19(15-24)	122(110-135)	104(90-120)	62(54-70)	30(20-38)	22(15-29)	18(14-2
Full oral feeding, days median(IQR)	49(40-59)	155(140-170)	140(125-158)	112(99-125)	83(70-95)	61(50-75)	50(40-6
Probiotics	326(10.7)	4(3.8)	13(6.7)	16(6.9)	38(11.6)	56(14.6)	44(9.8
Caffein	2709(89)	96(92.3)	184(95.3)	221(96)	321(98.7)	365(95.8)	426(95.
Duration of caffeine, days median(IQR)	36(30-42)	28(24-32)	37(30-42)	43(35-50)	45(40-50)	46(42-52)	39(32-4
Duration of hospitalization, days median(IQR) **Duration of hospitalization in survivors** **Duration of hospitalization in non-survivors**	 56(40-73) 18(8-28)	 133(110-150) 12 (6-20)	 114(98-135) 19(10-30)	 100(80-120) 17(9-26)	 80(65-96) 23(12-35)	 70(60-82) 22(10-36)	 61(50-7 16(9-25

Abbreviations: DR, delivery room; IQR, Interquartile Range; LISA, less invasive surfactant administration; MIST, minimal invasive surfactant therapy; NICU, neonatal intensive care unit

Table 3. Incidences of prematurity-related neonatal morbidities

Gestational week	Total n(%)	23 n(%)	24 n(%)	25 n(%)	26 n(%)	27 n(%)	28 n(%)	
Number of infants	3042 (100)	104 (3.4)	193 (6.3)	230 (7.6)	325 (10.6)	381 (12.5)	446 (14.6)	

ARTICLE IN PRESS

RDS	2324(76.3)	104(100)	187(96.8)	213(92.6)	292(89.8)	327(85.8)	378(84.7)	33
BPD **Death before BPD**	633(20.8)	83(79.8)	121(62.6)	104(45.2)	102(31.3)	75(19.7)	79(17.7)	3
diagnosis	1207(39.6)	1(0.9)	)	7(3)	37(11.3)	86(22.6)	143(32)	26
None	1202	20	1(0.5)	119 (51.7)	186(57.2)	220(57.7)	224(50.2)	16
Diagnosis	(39.5)	(19.2)	71	44(19.1)	87(26.7)	116(30.4)	108(24.2)	8
Mild	524(17.2)	3(2.8)	(36.7)	25(10.8)	33(10.1)	36(9.4)	51(11.4)	3
Moderate	231(7.6)	4(3.8)	17(8.8)	50(21.7)	66(20.3)	68(17.8)	65(14.6)	5
Severe	447	13(12.5)	16(8.2)					
	(14.7)		38(19.6)					
NEC **Death before NEC**	28 (0.9)	5(4.8)	6 (3.1)	4 (1.7)	4(1.2)	2 (0.5)	2 (0.4)	
diagnosis	2586(85)	89(80.7)	145(75)	181(78.7)	262(80)	318(83.5)	378(84.8)	4
None	428(14)	15(14.4)	42(21.7)	45(19.5)	59(18.1)	61(16)	66(14.8)	5
Diagnosis	177(5.8)	2(1.9)	11(5.7)	15(6.3)	19(5.9)	28(7.3)	30(6.7)	3
Stage I	155(5)	3(2.8)	18(9.3)	12(5.2)	24(7.4)	22(5.6)	22(4.9)	1
Stage II	96(3.1)	10(9.6)	13(6.7)	18(8)	16(4.9)	11(2.8)	14(3.1)	
Stage III								
ROP **Death before ROP**	102(3.3)	10(9.6)	24(12.4)	15(6.5)	15(46.1)	18(4.7)	10(2.2)	
examination	2177(71.5)	74(71.1)	107(55.4)	123(53.5)	199(61.2)	218(57.2)	319(71.5)	35
None	763(25)	20(19.3)	)	92(40)	111(34.7)	145(38.1)	117(26.3)	10
Diagnosis	148(4.8)	9(8.7)	62(32.1)	35(15.2)	23(7.1)	16(4.2)	11(2.5)	1
Anti-VEGF treatment	97(3.2)	8(7.7)	32(16.6)	11(4.8)	16(4.9)	23(6)	15(3.4)	
Laser photocoagulation	6(0.2)	1(1)	9(4.7)	1(0.4)	-	1(0.3)	1(0.2)	
Surgical treatment of ROP			2(1)					
hsPDA **Death before ECHO**	166(5.4)	36(34.6)	38(19.7)	28(12.1)	20(6.2)	20(5.2)	10(2.2)	
None	1920(63.1)	21(20.2)	55(28.5)	78(33.9)	150(46.2)	214(56.1)	282(63.2)	33
Diagnosis	956(31.5)	47(45.2)	100(51.8)	124(54)	155(47.6)	147(38.7)	154(34.6)	12
			)					
Sepsis **Sepsis episodes**	1695(55.7)	59(56.7)	126(65.3)	160(69.5)	220(67.7)	257(6.7)	255(57.1)	25
Early neonatal	589(19.3)	25(24)	)	64(27.8)	71(21.8)	85(22.3)	76(17)	8
sepsis	1357(44.6)	39(37.5)	54(28)	124(53.7)	186(57.2)	214(56.2)	213(47.9)	20
Late neonatal sepsis			92(47.7)					
IVH **None**	2192(72)	53(51)	92(47.7)	128(55.7)	191(58.8)	262(68.8)	328(73.5)	36
Stage I	360(11.8)	8(7.7)	33(17)	34(14.8)	45(13.8)	46(12)	55(12.3)	5
Stage II	194(6.3)	13(12.5)	24(12.4)	17(7.4)	37(11.4)	32(8.4)	27(6)	2
Stage III	142(4.6)	13(12.5)	26(13.5)	27(11.7)	25(7.7)	20(5.2)	17(3.8)	1
Stage IV	125(4.1)	17(16.3)	14(7.3)	22(9.6)	24(7.4)	19(4.9)	12(2.7)	1
PVL	29(0,9)	-	4(2)	2(0.9)	3(0.9)	2(0.5)	7(1.6)	

Abbreviations: BPD, bronchopulmonary dysplasia; ECHO, echocardiography, hsPDA, hemodynamic significant patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity; VEGF, Vascular endothelial growth factor

Table 4. Survival without major morbidity and mortality rates

Gestational week	Total n(%)	23 n(%)	24 n(%)	25 n(%)	26 n(%)	27 n(%)	28 n(%)

ARTICLE IN PRESS

Number of infants	3042	104	193	230	325	381	446
Survival	2381(78.2)	19(18.2)	66(34.2)	123(53.5)	218(67.1)	303(79.5)	365(81.8)
Survival without major morbidity	1301(42.8)	-	13(7.1)	28(12.4)	72(22.3)	133(35.4)	183(41.2)
Major morbidities affecting survival **IVH ≥ grade 3 or cystic PVL** **BPD** **NEC ≥ stage 2** **Sepsis** **ROP ≥ stage 3**	296(9.7) 1202(39.5) 251(8.3) 1695(55.7) 251(8.3)	30(2.9) 20(19.2) 13(12.5) 59(56.7) 18(17.3)	44(22.8) 61(31.6) 31(16) 126(65.3) 43(22.2)	51(22.1) 119(51.7) 30(13) 160(69.5) 47(20.4)	52(16) 186(57.2) 40(12.3) 220(67.7) 39(12)	41(10.7) 220(57.7) 33(8.6) 257(6.7) 40(10.5)	36(8) 224(50.2) 36(8) 255(57.1) 27(6)
Mortality	661 (21.7)	85(81.7)	127(65.8)	107(46.5)	107(32.9)	78(20.5)	81(18.2)
Early mortality (1-6 days)	386 (12.7)	53(50.9)	80(41.4)	60(26)	63(19.3)	48(12.5)	41(9.1)
Late mortality (7-28 days)	188(6.2)	26(25)	28(14.5)	33(14.3)	26(8)	22(5.8)	30(6.7)
Post-neonatal mortality (day 29 to until discharge)	87(2.9)	6(5.8)	19(9.8)	14(6)	18(5.5)	8(2.1)	10(2.2)

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.

Table 5. Multivariate logistic regression analysis for mortality, NEC, and severe IVH in infants ≤28 weeks of gestational age

	Mortality (aOR, 95% CI)	**p-value**	**NEC (aOR, 95% CI)**	**p-value**	**Severe IVH (aOR CI)**
(per 1-week decrease)	1.45 (1.30–1.62)	**<0.001**	1.20 (1.08–1.34)	**0.001**	1.32 (1.18–1.4
er 100 g decrease)	1.28 (1.18–1.39)	**<0.001**	1.15 (1.05–1.26)	**0.003**	1.22 (1.12–1.3
tilation (first 7 days, per	1.12 (1.06–1.18)	**<0.001**	1.08 (1.03–1.14)	**0.002**	1.10 (1.05–1.1
s	2.10 (1.65–2.68)	**<0.001**	1.85 (1.42–2.41)	**<0.001**	1.40 (1.10–1.7
ids (any use)	0.68 (0.54–0.85)	**0.001**	0.75 (0.60–0.95)	**0.02**	0.70 (0.55–0.8

ARTICLE IN PRESS

	1.22 (0.98–1.52)	0.07	1.10 (0.88–1.38)	0.40	1.18 (0.95–1.4

Abbreviations: IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis

ARTICLE IN PRESS