TITLE: INFLUENCE OF SEX IN MORBIDITY AND MORTALITY AMONG VERY-LOW-BIRTH-WEIGHT INFANTS LESS THAN 30 WEEKS GESTATIONAL AGE.

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CONTENT:
Accumulated evidence has shown female advantage in clinical outcomes in Very-Low-Birth-Weight (VLBW) infants. Not all previous studies considered perinatal confounding factors. In addition, it has been suggested that recent progress in perinatal care might have benefited males relatively more than females and changed differences in morbidity and mortality. The aim of our study was to determine whether sex differences in morbidity, mortality, and survival without major morbidity among VLBW infants under 30 weeks gestational age (GA), adjusting for perinatal risk factors, still persist considering the improvement in perinatal care, in two large cohorts of premature infants.

Retrospective analysis of prospectively collected data of VLBW infants, born at 240 to 306 weeks GA between January 2013 and December 2016 in the collaborative centers of the Spanish Neonatology Society (SEN1500) and in the South American Collaborative Neonatal (NEOCOSUR) Networks. The following patients were excluded: 173 infants (1.6%) who died in the delivery room, 467 (4.2%) with major congenital anomalies (74 of them died in delivery room), and six infants with ambiguous genitalia or whose sex was not properly recorded. Differences between sexes were compared by multivariate logistic regression analyses adjusting for confounding factors, and results are expressed as OR and 95% CI.

During the study period, 11,140 VLBW inborn infants were recorded in the study centers, 6,385 (57.3%) in the SEN1500 network and 4,755 (42.7%) in Neocosur. After exclusions, 10,568 patients were analyzed. Mean (SD) GA was 27.7 (1.8) weeks; birth weight 1023.1 (257.4) g; male sex: 53.2%; multiples: 28.1%. The table summarizes morbidity and survival odds of female vs. males, after adjusting for confounders.

After adjusting for GA, BW, multiple gestation, antenatal steroids, chorioamnionitis, maternal hypertension, maternal antibiotics, premature rupture of membranes, Cesarean section, advanced neonatal resuscitation and Network of origin, female infants had a lower risk of respiratory morbidity, NEC, and brain damage, and a higher likelihood of survival and survival without major morbidity.
Images:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=a4643c8e5deafb106c9d3ff0a0b4303f-MjAxOS0wNSM1Y2UyNjY2YzAwZTM3

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TITLE: MORTALITY PREDICTION IN VERY LOW BIRTH WEIGHT NEONATES USING THREE NEW PREDICTIVE MODELS

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CONTENT:

Preterm birth is the main cause of perinatal mortality. Decisions regarding care and treatment of these infants are specially challenging for health care professionals and families. Several predictive models for preterm mortality have been developed. Some of them are widely used throughout the world (CRIB score, NICHD model), however very few have been validated in other populations. In Spain, SEN1500 database includes data from over 2500 very low birth weight preterm infants per year born in our country. The aim of this study was to develop and validate different mortality predictive models for preterm infants registered in the SEN1500 database.

Inclusion: Infants born alive with birth weight < 1500 g or gestational age < 30 weeks admitted to 65 Spanish Neonatal Units and registered in SEN1500 database. Exclusion: fetal or delivery room deaths, major congenital defects or chromosomal abnormalities. Periods: “Development” of predictive models (2009-12) and “Validation” (2013-15). Predictive mortality models: Model 1 (prenatal), model 2 (first 24 hours of life), and model 3 (during hospital admission). Statistical analysis: dependent variable: hospital mortality. Significant independent variables were used in multivariable regression models. To establish the cut-off point between “death” and “no death”, Kappa indexes were used. Specificity, sensitivity, accuracy and area under the curve (AUC) were calculated for the 3 models.

14953 newborns were included, 8734 in the development phase and 6219 in the validation phase. 2015 of the included infants died, 373 (18.5%) before 24 hours of life, 1315 (65.3%) during the first month of life and 327 (16.2%) between 30 days of life and final discharge.

In the development phase, AUC to predict mortality was 0.833 (95% CI: 0.821-0.845) (p<0.001) in model 1 and 0.872 (95% CI: 0.860-0.884) (p=0.001) in model 2. In model 3, AUC to predict mortality was 0.999 (95% CI: 0.998-0.999) (p<0.001) for the first month of life and 0.950 (95% CI: 0.930-0.961) (p<0.001) after 30 days of life.

Cut off values for the different models, concordance (Kappa index) and prediction accuracy in the validation phase are shown in Table 1. Models 1 and 2 showed a “moderate” concordance, whilst in model 3 concordance was “very good”.

A national cohort of preterm patients was used to develop and validate three new mortality predictive models to be used in the prenatal period, first day of life and during hospital admission. Use of dynamic models of changing probability to predict individual mortality can improve outcome accuracy.

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**ID:** 375  
**TITLE:** PUBERTAL GROWTH OF CHILDREN BORN PRETERM  
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**CONTENT:**

Preterm birth (<37 gestational weeks) is associated with elevated levels of cardiometabolic risk factors in adulthood. Prematurity also affects early growth and preterm born children appear to be shorter as adults than those born at term. In addition, earlier puberty is associated with higher risk of cardiovascular disease in term born adults. As compared to term born controls, earlier pubertal growth was indeed detected in preterm and very low birth weight (VLBW) adolescents. Whether preterm birth across the whole range of gestational ages would also predict earlier pubertal growth, remains to be studied.

Growth data for the ESTER Preterm Birth Study were obtained from school healthcare (where most Finnish children are measured) annually until age 16 years, with final height measured at >19.9 years. We included subjects with ≥3 height measurements available above 6/7 years in girls/boys, and 15 severely disabled subjects were excluded. The analysis included 131/92/52 men and 147/105/51 women born term (≥37) / late preterm (34+0 to 36+6) / early preterm (<34 gestational weeks) respectively. To study group differences in pubertal growth we used SuperImposition by Translation And Rotation (SITAR), a mixed effects growth curve model that summarizes pubertal growth with a fitted mean curve and three subject-specific random effects: body size, tempo, and velocity. The models were unadjusted.

Final height was similar in all men, mean 177.6 (SD 7.2) / 178.0 (SD 6.8) / 178.0 (SD 6.9) cm, and in all women, mean 163.7 (SD 5.9) / 164.3 (SD 5.7) / 163.8 (SD 5.6) cm born term/late preterm/early preterm. When comparing the pubertal growth of early and late preterm groups (separately for men and women) to those born at term, no differences appeared in body size, growth tempo, or velocity (Figure). Mean age at peak height velocity was similar in all gestational age groups: 13.5 (SD 1.0) / 13.6 (SD 0.9) / 13.6 (SD 0.9) years in men and 11.8 (SD 0.9) / 11.8 (SD 0.7) / 11.8 (SD 0.8) years in women (Figure). Mean peak height velocity was also similar in all groups: 9.7 (SD 1.0) / 9.7 (SD 1.1) / 9.8 (SD 0.9) cm/year in men and 7.6 (SD 0.8) / 7.6 (SD 0.7) / 7.6 (SD 0.8) cm/year in women (Figure).

Against our hypothesis and other findings with preterm and VLBW children, neither early nor late preterm born children as a group displayed advanced pubertal growth spurt or other differences in pubertal growth compared to those born at term. We are currently pursuing analyses in subgroups including those defined by narrower strata of gestational age and birth weight SD score.
Figure. Velocity of growth in term (≥37), late preterm (34+0 to 36+6), and early preterm (<34 gestational weeks) groups of men and women. The curves were obtained from the Superimposition by Translation And Rotation (SITAR) analysis. No differences in pubertal growth were seen between the groups either in men or women. Mean age at peak height velocity in men born at term was 13.5 (SD 1.0) years, late preterm 13.6 (SD 0.9) years (difference to term-born men +0.11 years, 95% CI: -0.15, 0.37), and early preterm 13.6 (SD 0.9) years (difference to term-born men +0.04 years, 95% CI: -0.27, 0.36). Mean age at peak height velocity in women born at term was 11.8 (SD 0.9) years, late preterm 11.8 (SD 0.7) years (difference to term-born women -0.05 years, 95% CI: -0.26, 0.16), and early preterm 11.8 (SD 0.8) years (difference to term-born women +0.01 years (95% CI: -0.26, 0.28). Mean peak height velocity in men born at term was 9.7 (SD 1.0) cm/year, late preterm 9.7 (SD 1.1) cm/year (relative difference to term-born men +0.6%, 95% CI: -3%, 4%), and early preterm 9.8 (SD 0.9) cm/year (relative difference to term-born men +2%, 95% CI: -2%, 5%). Mean peak height velocity in women born at term was 7.6 (SD 0.8) cm/year, late preterm 7.6 (SD 0.7) cm/year (relative difference to term-born women -0.5%, 95% CI: -3%, 2%), and early preterm 7.6 (SD 0.8) cm/year (relative difference to term-born women -0.9%, 95% CI: -4%, 2%).

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TITLE: MEASURING EXTRAUTERINE GROWTH RESTRICTION IN VERY PRETERM INFANTS: DOES CHOICE OF REFERENCE MATTER?

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CONTENT:

Extrauterine growth restriction (EUGR) among children born very preterm (VPT) is a risk factor for poor neurodevelopmental outcome. It is commonly defined as a weight for postmenstrual age (PMA) less than the 10th percentile of postnatal growth references. Fenton's postnatal references, derived by meta-analysis of national birthweight and child growth charts, are commonly used in clinical care and research. Recently, the Intergrowth (IG) 21st project proposed alternative curves derived from multinational healthy preterm infants based on the assumption that normal growth in very preterm populations differs from the in-utero development of term children. We used these two approaches to investigate EUGR prevalence in a multinational sample of European VPT infants.

Data come from the EPICE (Effective Perinatal Intensive Care in Europe) project, a prospective multinational population based observational study in 19 regions from 11 European countries covering 850,000 annual. We included 6,351 infants discharged home or to domiciliary care before 50 weeks PMA. Neonates with missing PMA, discharged place and weight at discharge were excluded from the analysis. EUGR was defined as weight at discharge for PMA and sex < 10th percentile using Fenton and IG references. We compared the prevalence of EUGR by selected neonatal characteristics and country of birth, using X2 tests. We used generalized linear regression models with a Poisson distribution and robust standard errors to estimate adjusted risk ratios (aRR).

Mothers were on average 30 years old among which 57% were nulliparous and 68% had singleton deliveries. The prevalence of EUGR using Fenton’s references was 44.67% for boys and 46.14% for girls (NS) compared to 33.6% for boys and 25.5% for girls for IG (p< .01). Prevalence of EUGR by country ranged from 24.7% in Sweden to 60.5% in Portugal for Fenton and from 13.6% in Sweden to 42.7% in Portugal for IG as shown on the graph. Lower gestational age at birth, being SGA at birth and having a severe neonatal morbidity were risk factors for being EUGR, regardless of the reference. Boys were more growth restricted than girls when using IG, but not Fenton. Adjusting for case-mix did not reduce variability between regions: the aRR for EUGR for Portuguese compared to Swedish VPT infants was 2.5 (95% confidence interval (CI): 2.0-3.1) for Fenton and 3.3 (95% CI: 2.6-4.6) for IG.

Accurately identifying infants with sub-optimal growth is important for clinical care and for research on the etiology and consequences of EUGR. The difference in EUGR prevalence linked to choice of reference as well as the large variations between countries suggest that references should be validated in their target populations before adoption.

IMAGES: 
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