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Morbidity in ≤1500-Gram Births in Spain, 1993-2011: Study of a Sample of 1200 Cases

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Abstract

Background and Objective. Preterm birth has a major impact on growth, and very preterm birth is associated with disabilities in numerous developmental domains. This article describes and quantifies morbidities in a sample of 1200 ≤1500-g births in Spain between 1993 and 2011 based on parent information, and it highlights several variables that influence these morbidities. *Methods.* Multiple method surveys using computer-assisted telephones interviewing and computer-assisted web interviewing methods. Sample design was intentional. Most subjects were contacted via their referral hospitals. Data collection was done from April 2013 to June 2014. Prior to the survey, extensive qualitative fieldwork was conducted, including nonparticipant observation in neonatal units and the design and analysis of discussion groups and interviews with professionals and families, including preterm adolescents. *Results.* A total of 44.2% of the sample were experiencing morbidity (mean: 1.788 morbidities per child). The most prevalent types were learning difficulties (34.4%) and attention deficit/hyperactivity disorder (31.5%). The most influential variables were male gender, age, lower birthweight, private hospital admission for birth, scarcity of health resources in the family's residential area, non-Spanish maternal birthplace, and emotional distress in the primary carer. *Conclusions.* Overall, the total percentage of very low birth weight children with morbidities has decreased moderately between 1993 and 2011, thanks to major socio-sanitary improvements during this period. Biological and medical variables, rather than family factors, explain more accurately the presence of morbidities in children with birth weight ≤1500 g.

Keywords

morbidity of very preterm infants, very-low-birth-weight, prematurity

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Introduction

Prematurity is a neonatal condition that affects many growth-regulating factors. Health issues in premature infants are generally inversely proportional to weight and gestational age (GA), although there is a risk gradient for all preterm infants, including early births (GA 37 and 38).

The biological immaturity of individuals with very low birth weight (VLBW; individuals born with weight ≤1500 g) is the basis for morbidities that can appear at any time during their development, even in adulthood.[1-7] For this reason, experts[8,9] and parents' associations[10] insist that VLBW infants require close socio-health and education monitoring to minimize morbidity incidents and their severity.

In Spain, between 1993 and 2011, VLBW cases increased by 123% (National Statistical Institute [INE]). Despite this significant rise, the survival rate has improved substantially, especially since 2005[11,12] although morbidity episodes have not decreased to the same extent, neither in Spain nor in other countries, especially in the group of extreme preterm infants.[13-15] Hence, there is need for the most detailed information possible

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about morbidity and the variables that influence its occurrence in this group. This sociological study aims to improve factual knowledge about these issues, as it goes beyond clinical parameters and variables. To the best of our knowledge, this is the first research of this type in Spain.

Methods

A cross-sectional correlational study was made of VLBW infants born in Spain between 1993 and 2011. The aim was to identify the main biopsychosocial problems during growth (0-19 years), including episodes of morbidity, and detect connections with socio-family profiles and some of the changes that have occurred during this period in the socio-health care of these minors.

The lack of a frame for a probabilistic sample forced this sample design to be intentional. The sample group was primarily contacted via referral hospitals for VLBW infants. The sample consisted of 1202 valid interviews (1190 after weighting the data).

Data collection was done from April 2013 to June 2014, with a multimethod survey using computer-assisted telephone interviews and computer-assisted web interviews. Prior to the survey, extensive qualitative fieldwork was done, including nonparticipant observation in neonatal units (NU) and the design and analysis of 4 discussion groups and 25 in-depth interviews with professionals and families, including preterm adolescents. The qualitative material was used to design the self-administered structured questionnaire—with some open-ended questions—and to assist the subsequent interpretation of the survey data.

Data were analyzed using the SPSSWIN program, with a prior rebalance of the sample* from the "birth weight" and "year of birth" variables using data supplied by the INE.

*The most relevant features of the sample were the following: Neonates—males: 49.3%; average weight at birth: 1152.2 g; <1000 g at birth: 25.5% of the sample (8% <750 g, 17.5% 750-999 g). Mean GA at birth: 29.4 weeks (8.8% of births between weeks 22 and 25). Neonates <1500 g and >32 GA: 19.7%. Pregnancy: single 62.7%, multiple 37.3% (28.7% twins, 8.6% triplets or more; in 13.4% of multiple births, one of the siblings died in the NU). Birthing hospital ownership: public 91.4%, private 6.3%, mixed public-private management 2.3%. Mothers—age: 72.2% >30 years, 25.18% >35 years; 24.17% had undertaken infertility treatment and/or assisted reproduction; born in Spain: 94.3% (95% of partners born in Spain); breastfeeding: 60.4%.

Results

Description and Quantification of VLBW Infant Morbidity

Very preterm birth is associated with disabilities in multiple developmental domains.[16] The total percentage of children with morbidities in our survey was 44.2%, much higher than for the total population in Spain for this age (1.9%, in the Disability, Personal Independence and Dependency Survey, EDAD 2008),[17] with a mean morbidity incidence of 1.788 per child. Of the total sample, only 8.4% suffered temporary morbidity, 13.5% suffered permanent morbidity, 10.9% morbidities of both types, and 11.2% had a type of morbidity not included in our list.

Table 1 shows that the most frequent types of morbidity appear late in growth. High prevalence and low severity dysfunctions such as learning difficulties (34.4%) and behavioral problems such as attention deficit/hyperactivity disorder (31.5%) roughly concur with findings in other studies.[4,18,19]

Infant cerebral palsy, often with serious consequences, has declined[20] or remained stable despite the increase in survival of large preterm infants.[21] In our sample, it declined, albeit not significantly.

For this study, we hypothesized that basic improvements in the survival and health of VLBW individuals occurred in Spain since 1998 due to the use of new treatments (prenatal corticosteroids, surfactants, nutritional optimization, nasal continuous positive airway pressure devices, etc), the gradual introduction since 2004 of the family-centered care model, which became the predominant model in NU at Spanish public hospitals as of 2009, and the protocolized medical follow-up of all VLBW cases, especially at public hospitals; although the public cover of early childhood intervention and rehabilitation programs is less widespread. To check this hypothesis, we seek a relationship between the children's "year of birth" and the morbidities they suffer.

Table 2 shows the percentage of morbidities in this population as a function of the defined breakdown by years. As hypothesized, the total percentage of children with morbidities has decreased moderately, although caution is advisable in the interpretation of the data for those born between 2009 and 2011 given the difficulty of an accurate diagnosis of the most prevalent morbidities in this population before the age of 3 to 4 years.

Morbidity trends (Table 3) and other data from our study show the following:

- Overall, health disorders decreased moderately between 1993 and 2011 (Kendall's Tau-*c* is −.077

Table 1. Frequency of Morbidity Types (Temporary and Permanent)[a].

Type of Morbidity	Response		Percentage of Cases
	n	Percentage	
Learning difficulties (TM)	173	19.3	34.4
Dyslexia (TM)	11	1.2	2.2
Simple language delay (TM)	102	11.4	20.3
Specific language disorder (TM)	24	2.7	4.8
Psychomotor instability syndrome (TM)	21	2.4	4.3
Autism spectrum disorder (PMD)	9	1.0	1.9
Generalized developmental disorder (PM)	45	5.0	8.9
Attention deficit/ hyperactivity disorder (PM)	158	17.6	31.5
Cerebral palsy (PM)	59	6.6	11.7
Visual impairment (PM)	101	11.2	20.0
Hearing impairment (PM)	39	4.3	7.7
Intellectual disability (PM)	29	3.3	5.8
Others	127	14.1	25.3
Total	899	100.0	178.8

Abbreviations: TM, temporary morbidities; PMD, persons with multiple disabilities; PM, permanent morbidities.
[a]It should be noted that the term "morbidities," little known outside professional circles, was not used in this research project's questionnaires. Instead, to make it easier for families to understand, we used "sequela," hence the appearance of "sequelae" in some of the tables. Nevertheless, the term "morbidities" is used in this article as we consider that methodologically it is not possible to speak of "sequelae" unless there is a control group, although this distinction is not made in many studies.

and Spearman rank correlation is −.067) among subjects with ≤1500 g at birth, as did those with <1000 g at birth, despite the greater survival rate of increasingly immature babies.[22]

- Learning and attention difficulties, "invisible disabilities,"[23] were the most prevalent morbidities in this population. Although 87.3% VLBW infants entered the standard education system, 41.3% needed some kind of help during their schooling. Among the latter, 56.0% needed teacher support at school, 42.2% educational reinforcement, 18.6% curricular adaptation, 22.7% rehabilitation and/or physiotherapy, 51.3% speech therapy, and 25.0% psychological support.
- An increase was detected in nonpermanent morbidity—may be because they were better understood and hence easier to diagnose—along with a decrease in permanent morbidity, no doubt due to advances in perinatal care and the therapeutic medical treatment received by these children.[‡]

Variables That Influence Morbidity

Our study analyzed 3 types of variables: *biological variables* (neonatal sex, birth year, weight at birth, GA, type of pregnancy, maternal use of fertility treatments, assisted reproduction, etc), *medical and care service variables* (time in neonatal intensive care unit and/or NU time, hospital ownership, family-centered care practices, medical monitoring due to prematurity, shortage of specialized sanitary resources in the locality of family residence, early stimulation and rehabilitation programs and treatments, hospital readmissions, etc), and *socio-family variables* (total number of offspring, age, nationality, civil status, educational achievement and employment status of both parents, town size where the family lives, income, resources and support for the family, emotional distress in the primary carer, etc).

A logistic regression causal model was designed to study the influence of these variables, in which the dependent variable was the presence/absence of morbidities in the child.[‡] The most notable result (Table 4) is that the majority of the variables carried little weight in explaining the presence/absence of morbidities in this population. These results match the nonclinical approach of our study, which did not collect specific data on the prevalence of pathologies with a major effect on morbidity trends in this population (periventricular-intraventricular hemorrhage, bronchopulmonary dysplasia, retinopathy of prematurity, etc.), nor congenital deficiencies or problems during labor, the latter two explaining 44% and 13%, respectively, of cases in the under 20 years age group with deficiencies in Spain.[17] However, this does not mean that the variables analyzed in our study did not exert some influence.

The results of our model in relation to the biological variables show that subjects born with less weight, less GA, and born earlier have a higher risk of morbidities (statistically significant relationships). Birth weight was the variable with the greatest influence of all 3 factors on the explanation of the presence of morbidities in this population.[24] Male sex was another very relevant biological variable.[25-27]

[‡]We consider that the high percentage of simple language delay of those born between 2009 and 2011 largely expresses the characteristic maturing delay of large preterms.
[‡]Variables such as duration in the neonatal intensive care unit or hospital readmissions were excluded from the analysis as they were not necessarily independent of previous morbidities such as those of a congenital nature, for example.

Table 2. Frequency of Morbidities by Date of Birth (1993-2011).

		Date of Child's Birth				
		1993-1998	1999-2003	2004-2008	2009-2011	Total
Children with morbidities	% in year span	52.7	41.6	44.0	38.9	44.2
	Number	237	281	375	244	1137

Table 3. Morbidity Trends (1993-2011).

Type of Morbidity	1993-1998	1999-2003	2004-2008	2009-2011	Total	ρ	Sig.
Learning difficulties	20.5%	20.0%	12.6%	8.5%	173	− 0.139	.000
Dyslexia	3.5%	0.7%	0.1%	0.0%	11	−0.117	.000
Simple delay of language	6.7%	2.3%	9.6%	18.1%	102	−0.145	.000
Specific language disorder	2.0%	2.4%	1.7%	2.5%	24	−0.006	.845
Psychomotor instability syndrome	2.0%	0.2%	2.6%	2.5%	21	0.027	.343
Autism spectrum disorder	2.2%	0.6%	0.2%	0.7%	9	−0.049	.093
Generalized developmental disorder	6.7%	2.4%	2.8%	4.9%	45	−0.030	.293
Attention deficit/hyperactivity disorder	24.0%	15.2%	10.9%	7.1%	158	−0.173	.000
Cerebral palsy	6.0%	5.3%	5.0%	4.5%	59	−0.028	.343
Visual impairment	12.0%	8.2%	9.2%	6.0%	101	−0.063	.029
Hearing impairment	4.6%	2.5%	3.8%	2.8%	39	−0.024	.402
Intellectual disability	6.3%	2.7%	1.0%	1.2%	29	−0.112	.000
Others	10.4%	12.5%	10.8%	10.8%	127	−0.017	.566
No morbidities	47.2%	58.3%	56.1%	61.0%	636	0.076	.010
Total	237	281	375	245	1138		

Before assessing the role played by the other 2 sets of variables, it is important to note that 16.1% of VLBW individuals did not participate in any developmental follow-up program after being discharged from the NU, despite the high biological risk in each case. The majority of these individuals were born in a private hospital (24.3% with no follow-ups vs 15.6% in the case of those born in public hospitals), their mother was not born in Spain (19.7% vs 15.8% with a Spanish mother), and had a lower education level, lived in towns of <100 000 inhabitants, where there are fewer specialized health resources and development programs, and were part of a lower income family.

Among the medical and care service variables, hospital ownership, particularly private hospitals, carried considerable weight in explaining morbidities; 43.0% of children born in public hospitals, 40.0% of those born in mixed-management hospitals, and 63.4% of those born in private hospital reported morbidities (in private hospitals there are also more Caesarean sections and preterm individuals participate less in growth monitoring programs).

Two socio-family variables stand out. Emotional distress in the primary carer after the baby's release from the NU is an influential factor in VLBW morbidities, as pointed out by Spanish pediatricians.[28] In preterm infants, cognitive development and behavioral outcomes correlate negatively with maternal depression and anxiety.[29] Another relevant factor is the case of non–Spanish-born mothers—the largest number were born in Central and South America (2.9% of the total). The probability of morbidity increases if both parents were not born in Spain.

Discussion

This last aspect raises an interesting issue for debate: the importance of providing families with caring support in order to mininize VLBW morbidity. Several studies have shown that the majority of immigrant women living in Spain are healthy, they have a lower incidence of risk practices during gestation, and their children show no more biological risk factors such as low weight at birth than others, even if they come from disadvantaged socioeconomic backgrounds and are socially disadvantaged in the host country. Other factors such as sociosanitary conditions which raise the risk of birth defects in the immigrant population may also be considered; however, most risk factors are probably related to what happens after birth and, above all, to insufficient

Table 4. Influence of Variables on the Presence/Absence of Repercussions (Morbidities)[a]. Logistic Regression Causal Model (Dependent Variable: "Presence/Absence of Repercussions").

Variables	B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)	
							Low	High
P5_a_01(1)—Male gender	0.913	.188	23.616	1	.000	2.492	1.724	3.602
P6_a—Birth year	–0.039	.017	5.160	1	.023	0.961	0.929	0.995
P8_a_2—Weight at birth	–0.002	.000	24.492	1	.000	0.998	0.998	0.999
P13_a_01(1)—Mother not born in Spain	1.181	.416	8.071	1	.004	3.258	1.442	7.359
P15_a_01(1)—Birth in a private hospital	1.175	.450	6.820	1	.009	3.240	1.341	7.828
P27_a_1—Emotional distress in primary carer	0.071	.028	6.552	1	.010	1.073	1.017	1.133
P27_a_10—Shortage of sanitary resources specialized in residence locality	0.067	.027	6.264	1	.012	1.069	1.015	1.127
Constant	1.168	.485	5.806	1	.016	3.214		

Abbreviation: CI, confidence interval.
[a]Our logistical regression model explained 20.5% (Nagelkerke's R^2) of the presence of morbidities. It correctly classified 66.2% of cases, with a sensitivity of 59.4% and a specificity of 71.9%.

support, either private or public,[*†] for coping with the complex,[30] and expensive[31] nurture process required by these children. These issues have a greater impact when the socio-family circumstances are more precarious due to social disadvantage, low income,[††] or education achievement, or difficulties in reconciling family and/or work obligations with the monitoring required by these children, and may help explain the impact of this maternal condition[32].

A degree of bias may have entered our results due to the sample structure, based on voluntary participation by subjects attended at referral hospitals, which often treat the most seriously affected VLBW infants; in fact, in relative terms, our sample has a larger percentage of males and infants with a shorter EG than the population of VLBW infants born in Spain in 1993 to 2011, according to INE.

Furthermore, our sample included adolescents, an important aspect given that health problems and deteriorating neurocognitive functions in VLBW infants can increase with age.[33] This is the first study to cover such a large population throughout Spain for the analysis of the main factors in the development of these children, and of the contextual factors that influence their morbidities, contributing to identify which children are in a situation of higher risk.

*Forty-six percent of families with VLBW children between 1993 and 2011 in Spain received no assistance whatsoever in the early months of their child's life, not even from their family network.

†Our results in this respect coincide with those of Brooks-Gunn[34] on intellectual quotient (IQ) scores in 5-year-old preterm children.

These aspects of our sample help explain why socio-family factors seem to have little influence on the incidence of morbidity in this population, while other variables and socio-sanitary conditions such as the type of hospital management or a lack of specialized health resources do carry considerable weight.

Another methodological problem is the lack of a sample framework for the population of VLBW infants and, with a view to improving the explanatory potential of such studies, the need to promote longitudinal sociological studies that can monitor the effect of memory/recollection in interviewees' answers to questions about the order of events in time, for example. Studies should also be designed to include more biological and medical variables, given the impact they seem to have on morbidities in VLBW individuals.

Key Messages

- The changes in health care between 1993 and 2011 in Spain have reduced morbidities moderately among infants with birth weight ≤1500 g.
- Learning difficulties and behavioral problems are the most prevalent morbidities in children with birth weight ≤1500 g.
- Biological and medical variables, rather than family factors, explain more accurately the presence of morbidities in children with birth weight ≤1500 g.
- It is necessary to provide families with support in order to minimize morbidity due to very low birth weight and other associated risk factors.

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Author Contributions

CGE: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
JJSC: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
FJGS: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
JMSG: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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