High Blood Pressure during Pregnancy is not a Protective Factor for Preterm Infants with Very Low Birth Weight. A Case-Control Study

Hipertensão arterial na gestação não é fator de proteção para recém-nascidos prematuros de muito baixo peso ao nascer. Um estudo caso controle

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Abstract

Objective To evaluate whether the presence of maternal blood pressure reduces the risks of morbidity, perinatal mortality and morbidity at 24 months of age in very low birth weight infants (VLBWIs) compared with a control group.

Methods A retrospective, observational, case-control study. Total 49 VLBWIs were allocated to the study group, called the maternal arterial hypertension group (AHG), and matched with 44 in the control group (CG). The infants were assessed during hospitalization and at 12 and 24 months corrected age at a specialized clinic. For the assessment of growth, the World Health Organization (WHO) Anthro software (Geneva, 2006) was used, and for the psychomotor assessment, the Denver II test was used.

Results In relation to the antenatal variables, the infants of the AHG had more centralized circulation assessed by Doppler, received more corticosteroids and magnesium sulfate, and were born by cesarean section more frequently. In terms of the postnatal and in-hospital outcomes, the AHG had a higher gestational age at birth (30.7 versus 29.6 weeks) and a lower frequency of 5-minute Apgar scores of less than 7 (26.5% versus 52.3%). The CG had a higher rate of pulmonary dysplasia (30.2% versus 8.3%). There were no differences in terms of hospital mortality, complications, somatic growth and functional problems at 24 months of corrected age.

Conclusion The presence of maternal hypertension, especially preeclampsia, was not a protective factor against morbidity, mortality and evolution in VLBWIs aged up to 24 months. Therefore, the clinical practice should be focused on prolonging the pregnancy for as long as possible in these conditions as well.

Keywords
- premature birth
- child development
- preeclampsia

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Resumo

Objetivo Avaliar se a presença de hipertensão arterial materna reduz os riscos de morbidade, mortalidade perinatal e morbidade aos 24 meses de idade em recém-nascidos de muito baixo peso (RNMBPs) em relação a um grupo controle.

Métodos Estudo retrospectivo, observacional, caso controle. Foram alocados 49 RNMBPs no grupo de estudo, chamado de grupo com hipertensão arterial materna (GHA), e 44 no grupo controle (GC), avaliados durante a internação hospitalar e aos 12 e 24 meses de idade corrigida em ambulatório especializado. Para avaliação do crescimento, foi adotado o programa WHO Anthro, e o teste de desenvolvimento de Denver II para a avaliação psicomotora.

Resultados Em relação às variáveis antenatais, fetos do GHA apresentaram mais centralização da circulação avaliada pelo Doppler, receberam mais corticosteroides e sulfato de magnésio, além de terem nascido mais por cesáreas. Quanto aos desfechos pós-natais e durante a internação, o GHA teve idade gestacional de nascimento maior (30,7 × 29,6 semanas) e menor frequência de boletim de Apgar no quinto minuto inferior a 7 (26,5% x 52,3%). Entre as complicações avaliadas, o GC teve maior frequência de displasia pulmonar (30,2 × 8,3%). Não houve diferenças em relação à mortalidade hospitalar, ao crescimento somático e às complicações funcionais aos 24 meses de idade corrigida.

Conclusão A presença de hipertensão arterial materna, em especial a pré-eclâmpsia, não foi fator de proteção quanto à morbidade, mortalidade e evolução até os 24 meses de idade em RNMBPs. Desta forma, a prática clínica deve ser voltada para garantir o maior prolongamento possível da gestação também nestas condições.

Palavras-chave

- nascimento prematuro
- desenvolvimento infantil
- pré-eclâmpsia

Introduction

Despite the advances in perinatal medicine, premature birth is still a serious health problem worldwide, and is the cause of significant levels of neonatal deaths and permanent limitations throughout the lives of the individuals affected.[1]

According to the information available in the Computer Science Department of The Brazilian Unified Health Care System (DATASUS, in the Portuguese acronym),[2] in the year 2013, there were 331,871 births in Brazil with a gestational age of between 22 and 36 weeks, corresponding to 11.4% of the total population of live births. In this same period, the births of 35,385 children weighing between 500 and 1499 g, defined as very low weight, were recorded.

In a hospital-based study conducted by a Brazilian research network, a rate of 12.3% of prematurity was identified in leading maternity units. The main causal factors were spontaneous premature labor in 36.0%, premature rupture of the membranes in 29.0%, and elective early labor in 35.0%. In the latter group, hypertensive syndromes during pregnancy were the main reasons for the induced labor.[3]

The population of newborns with birth weights below 1500 g, defined as very low birth weight infants (VLBWIs), represents a special class among premature births, as it is a group consisting of individuals with a higher individual risk for neonatal death and for the onset of definitive impairments of the neuromotor and cognitive skills, including cerebral palsy, learning difficulties, chronic lung disease and auditory and visual disorders.[4] As the possibilities of survival increase, so does the amount of follow-up these children require, placing a greater burden on the health care system.[5]

A population study conducted in Denmark found that among individuals born between 1974 and 1996, those born prematurely, or who suffered fetal growth restriction, presented a higher risk of hospitalization during adulthood, and this was linked to a catalog of diseases, including cardiovascular, endocrinal, neurological, obstetric, psychiatric, pulmonary and urological disorders.[6]

Identifying the cause of premature labor is of paramount importance, not only for short-term decision-making, but also for adopting interventions that can reduce the risk of future recurrence. The presence of arterial hypertension (AH) during pregnancy, particularly preeclampsia, represents a serious threat to maternal and fetal health, due to the maternal organic impairment and placental disorders it can cause.

It is calculated that each year, there are ~ 76,000 maternal and 500,000 perinatal deaths linked to preeclampsia worldwide.[7] The physiopathological process characterized by intense inflammation and endothelial dysfunction results in multiple organ failure, including placental changes that severely limit fetal development, and can lead to the death of both the mother and the child, if labor is not induced.[8] Therefore, induced or elective labor represents, in the majority of cases, the only alternative for safeguarding the interests of the mother and child.

In cases related to maternal AH, we see, in Brazil, that severe maternal morbidity is linked to the delayed adoption of effective interventions, including the timely interruption

of the pregnancy.[9] Based on a study that evaluates this issue, it can be inferred that this level of care has a direct impact on the conditions of birth, and increases the future risks.

It appears that there is no information available to identify whether, among the causal facts linked to the occurrence of premature labor, there are any specific conditions with a differentiated prognosis for immediate and later complications. This is a complex issue, due to the intricate web of variables that can affect the final outcomes.

We therefore believe that evaluating the early and late prognosis of VLBWIs due to elective prematurity associated with maternal AH, and comparing these outcomes with VLBWIs due to other maternal conditions, can contribute to this issue, offering some support for clinical decision-making in this area.

Methods

A retrospective, observational and analytical case control study was conducted at a hospital in the city of São Paulo that is part of the Brazilian Unified Health Care System (SUS, in the Portuguese acronym), linked to the Escola Paulista de Medicina [São Paulo School of Medicine]. The eligible population consisted of 125 VLBWIs born between January 2004 and December 2007. Out of this number, 93 VLBWIs met the inclusion criteria; 49 were allocated to the maternal AH group (AHG) and 44 to the control group (CG).

After discharge from the hospital, the infants were sent for follow-up at the outpatient department for premature babies, with the supervision of the Neonatal Pediatrics Department of the Escola Paulista de Medicina. The data were analyzed through a follow-up visit at between 12 and 24 months of corrected age; 28 children of the AHG completed this phase, and 21 of the CG did the same.

The exclusion criteria for both groups were the presence of at least one of these conditions, such as premature rupture of the membranes with clinical or laboratory signs of maternal or fetal infection, diabetes mellitus, premature dislocation of the placenta, placenta previa, multiple pregnancy and congenital malformation.

The maternal and fetal antenatal epidemiological data were analyzed, including maternal age, type of hypertensive syndrome, the cause of premature labor in the CG, fetal presentation, the type of labor, the use of antenatal corticosteroids (ACs) to accelerate fetal maturity, and the use of magnesium sulfate.

After birth, the outcomes related to the labor and the hospitalization period were analyzed, including birth weight, the 5-minute Apgar score, adequacy of weight for gestational age, gestational age, need for resuscitation in the labor room, respiratory discomfort syndrome, mechanical ventilation time, retinopathy of prematurity, ventricular hemorrhage, ventricular leukomalacia, necrotizing enterocolitis, sepsis, meningitis, bronchopulmonary dysplasia, hospitalization time, and in-hospital mortality.

The anthropometric data taken in the outpatient department included weight, length, and head circumference, taken at between 12 and 24 months of corrected age, calculated using the World Health Organization WHO Anthro software (Geneva, 2006), version 1.0.4 (available at: who-anthoplus.sharewarejunction.com), taking as reference the growth curves developed by the WHO (2006).[10] The Z Score (ZS) categories were adopted, defined as: $ZS < -2 =$ low for age; $-2 \leq ZS \leq +2 =$ adequate for age; and $+2 \leq ZS =$ high for age.

At 24 months of corrected age, the presence of neurological limitations was analyzed (muscle tone, convulsions), as well as auditory deficiencies (failure in the evoked otoacoustic emissions or brain stem auditory evoked potential tests) and limitations in psychomotor development, determined by the Denver II Developmental Screening Test.[11]

For the data analysis, Student's *t*-test was used for the averages, or the Mann-Whitney test for the comparisons between medians. For the categorical variables, the Chi-squared test or Fisher's exact test was used. In all of the analyses, a level of significance of $p < 0.05$ was used. The project was analyzed and approved by the Research Ethics Committee of the Universidade Federal de São Paulo, registered under opinion # 1799/2007.

Results

In the AHG, preeclampsia was present in 87.8% of the cases, whether in isolation or associated with chronic AH. In the CG, the main causes of the low birth weight were premature rupture of the membranes and spontaneous premature labor, both with a rate of 34.1%. The remaining causes were related to diverse conditions, such as acute fetal risk and cervical incompetence (►**Table 1**).

In terms of the conditions that precede labor, there were similarities in both groups in relation to maternal age and type of fetal presentation, but among the fetuses of the AHG, the presence of circulatory adaptation in response to placental insufficiency (fetal centralization) was statistically significant, as was the administration of ACs and magnesium

Table 1 Etiological factors related to prematurity in very low birth weight infants (VLBWIs) in the arterial hypertension group (AHG; $n = 49$) and in the control group (CG; $n = 44$)

Etiological factor	N	%
Arterial hypertension group		
Preeclampsia	33	67.3
Preeclampsia with CAH	10	20.5
Essential arterial hypertension	06	12.2
Total	49	100.0
Control group		
Premature rupture of the membranes	15	34.1
Spontaneous premature labor	15	34.1
Fetal risk	11	25.0
Maternal risk	03	6.8
Total	44	100.0

Abbreviation: CAH, chronic arterial hypertension.

Table 2 Maternal and antenatal variables in very low birth weight infants (VLBWIs) in the arterial hypertension group (AHG; $n = 49$) and in the control group (CG; $n = 44$)

Variable	AHG		CG		*p*
	n	%	n	%	
Maternal age[a]	28.8 ± 6.1		27.1 ± 7.3		0.240
Fetal presentation					
Cephalic	28	60.9	31	70.4	0.651
Breech	13	28.2	09	20.5	
Shoulder	05	10.9	04	9.0	
Centralization on Doppler	28	57.1	09	20.9	< 0.001*
Antenatal corticosteroids	45	91.8	32	72.7	0.015*
Magnesium sulfate	27	55.1	–	–	< 0.001*
Type of labor					
Vaginal	02	4.1	18	40.9	
Cesarean section	47	95.9	26	59.1	< 0.001*

[a]Note: Mean standard deviation, *significant *p* values.

sulfate. Cesarean sections were also more frequent in this group. In both groups, there were high rates of cesarean section: 95.9% in the AHG, and 59.1% in the CG (►**Table 2**).

In relation to the neonatal in-hospital outcomes, ►**Table 3** shows that both groups were similar in terms of birth weight and number of infants small for gestational age, the need for resuscitation in the labor room, the number of days of hospitalization, and the amount of time on assisted ventilation. However, the AHG showed significant differences in relation to gestational birth age (30.7 versus 29.6 weeks) and 5-minute Apgar score below 7 (26.5 versus 52.3%).

►**Table 3** also shows that the long period of hospitalization required the care of a significant number of neonatal complications, which were evenly distributed in both groups, with emphasis on the high rates of retinopathy of prematurity, ventricular hemorrhage and sepsis. Of the complications evaluated, a significant difference was detected: pulmonary dysplasia was less frequent in the AHG than in the CG (8.3 versus 30.2%).

In relation to in-hospital mortality, the rate of deaths in the general population was of 20.4%; the comparison between the groups did not show any significant differences; in the CG, the absolute number of deaths was practically double that of the AHG. The mortality rates also followed a similar

Table 3 Neonatal outcomes of very low birth weight infants (VLBWIs) in the arterial hypertension group (AHG; $n = 49$) and in the control group (CG; $n = 44$)

Variable	AHG		CG		*p*
	n	%	n	%	
Birth weight (grams)[a]	1,118.6 ± 275.4		1,096.6 ± 278.4		0.703
Gestational age[a]	30.7 ± 2.5		29.6 ± 2.6		0.044*
Days of hospitalization[b]	42.0 (1 – 96)		47.5 (1–174)		0.262
Days on ventilation[b]	09.0 (1–63)		11.5 (1 -174)		0.237
Apgar score < 7	13	26.5	23	52.3	0.011*
Small for GA	23	46.9	13	29.5	0.086
Resuscitation in labor	8	16.3	14	31.8	0.108
Respiratory discomfort	39	79.6	37	86.0	0.415
Retinopathy	34	82.9	26	74.3	0.357
Ventricular hemorrhage	24	51.1	15	36.6	0.173
Cerebral leukomalacia	3	6.4	2	4.7	0.099
Necrotizing enterocolitis	4	8.3	1	2.3	0.365
Sepsis	17	35.4	18	41.9	0.528
Meningitis	2	4.2	3	7.0	0.664
Pulmonary dysplasia	4	8.3	13	30.2	0.007*
Total hospital deaths	7	14.3	12	27.3	0.121
Deaths by weight category					
< 750 g	5/7	71.4	4/5	80.0	> 0.999
750 – 1,000 g	1/6	16.7	4/12	33.3	0.615
1,001 – 1,250 g	1/18	5.6	1/10	10.0	> 0.99
1,251 – 1,499 g	0/18	–	3/17	17.6	0.104

Abbreviation: GA, gestational age, [a]Note: Mean standard deviation; [b]median, maximum and minimum; *statistically significant.

Table 4 Z scores (ZS) calculated between 12 and 24 months of age in very low birth weight infants (VLBWIs), in the arterial hypertension group (AHG; $n = 49$) and in the control group (CG; $n = 44$)

Variable	AHG		CG		*p*
	n	%	n	%	
Weight for age (W/A)					0.639
ZS W/A < -2	2	7.1	3	14.3	
-2 ≤ ZS W/A ≤ +2	26	92.6	18	85.7	
Length for age (L/A)					0.443
ZS L/A < -2	3	10.7	4	19.1	
-2 ≤ ZS L/A ≤ +2	25	89.3	17	80.9	
Head circumference for age (HC/A)*					0.789
ZS HC/A < -2	–	–	1	5.0	
-2 ≤ ZS HC/A ≤ +2	25	89.3	17	85.0	
ZS HC/A > +2	3	10.7	2	10.0	

*Note: *20 controls evaluated.

pattern when analyzed by birth weight categories. Newborns weighing less than 750 g had markedly reduced chances of survival in both groups (61.4% versus 80.0%), and the risk of death was significantly reduced for infants weighing at least 1,000 g (►**Table 3**).

In relation to the outpatient evaluation, the loss to follow-up of 14 infants in the AHG and 11 in the CG is noted. In relation to the ZSs relative to somatic growth, the comparison between the groups did not identify any significant differences in relation to weight, length or head circumference for the age at the evaluation (►**Table 4**).

In terms of functional deficiencies, both groups showed similar rates of neurological, auditory and motor problems (►**Table 5**).

Discussion

Premature labor is the highest cause of neonatal morbidity and mortality worldwide. Various risk factors are associated with its occurrence. It is spontaneous in around 75.0% of cases, whether associated or not with the premature rupture of the membranes. The remaining cases are due to elective indications, mainly because of problems such as preeclampsia and placental insufficiency.[12]

Based on the results of a Brazilian multicenter trial[3] to evaluate the causes of premature labor in Brazil, using hospital information, we can consider that, in our country, 35.0% of premature births are the result of the elective interruption of the pregnancy, mainly due to complications associated with hypertensive states. In this same study, it was found that 21.0% of the births occurred at less than 32 weeks, an age range that includes very low birth weight infants (less than 1,500 g). Our results, although originating in a single center, are similar to those of the aforementioned study, in terms of causal factors, but it is not possible to affirm whether the outcomes seen in this specific population can be extrapolated on a wider scale.

Newborns in this weight category are part of a group that, from the very first moments of birth, depends on numerous

Table 5 Functional abnormalities at 24 months of life in very low birth weight infants (VLBWIs), according to birth weight categories, in the arterial hypertension group (AHG; $n = 28$) and in the control group (CG; $n = 21$)

Abnormality	AHG						CG						*p**
	yes		no		total		yes		no		total		
	n	%	n	%	n	%	n	%	n	%	n	%	
Neurological													
751 – 1,000 g	–	–	4	100.0	4	100.0	–	–	7	100.0	7	100.0	
1,001 – 1,250 g	2	20.0	8	80.0	10	100.0	2	33.3	4	66.7	6	100.0	0.604
1,251 – 1,499 g	1	7.1	13	92.9	14	100.0	2	25.0	6	75.0	8	100.0	0527
Total	3	10.7	25	89.3	28	100.0	4	19.0	17	81.0	21	100.0	0.443
Auditory													
751 – 1,000 g	–	–	4	100.0	4	100.0	–	–	7	100.0	7	100.0	
1,001 – 1,250 g	2	20.0	8	80.0	10	100.0	1	16.6	5	83.3	6	100.0	1.000
1,251 – 1,499 g	3	21.4	11	78.6	14	100.0	2	25.0	6	75.0	8	100.0	1.000
Total	5	17.9	23	82.1	28	100.0	3	14.3	18	85.7	21	100.0	> 0.999
Psychomotor													
751 – 1,000 g	1	25.0	3	75.0	4	100.0	1	14.3	6	85.7	7	100.0	1.000
1,001 – 1,250 g	2	20.0	8	80.0	10	100.0	1	16.6	5	83.3	6	100.0	1.000
1,251 – 1,499 g	2	14.2	12	85.7	14	100.0	3	37.5	5	62.5	8	100.0	0.309
Total	5	17.9	23	82.1	28	100.0	5	23.8	16	76.2	21	100.0	0.726

*Note: Fisher's exact test.

procedures to ensure their immediate survival and reduce later damage. Once critical situations have been overcome, there is a need for greater long-term hospitalization due to complications such as infections, necrotizing enterocolitis, lung problems due to ventilation, periventricular hemorrhage, leukomalacia and retinopathy of prematurity. In our study, we recorded a wide range of complications in both groups, with patients requiring hospitalization times of more than 40 days.

We did not identify any precise estimates of the amount of resources allocated by the Brazilian health care system for the care of premature newborns. An Italian study[13] calculated the specific hospital costs for the care of very low weight newborns, with an average hospitalization time of 59.7 days, estimating the individual hospital costs at 20,502.00 euros. Following this proportion, the estimated calculation in our population would be more than 60,000 Brazilian reais. A British study[14] with the same objectives stratified the costs by birth weight, obtaining an individual cost per newborn weighing less than 1,000 g of 26,815.00 pounds, which is equivalent to 152,845.00 Brazilian reais, and 18,817.00 pounds, which is equivalent to 107,256.00 Brazilian reais, for those with birth weights between 1,000 and 1,500 g.

In terms of the in-hospital complications detected, the groups showed similar rates for most of the variables. However, the CG showed more problems, as their gestational age at birth was lower, there was a higher rate of use of ACs, none of them received magnesium sulfate, they had poorer conditions in the 5-minute Apgar score, and they had higher rates of lung dysplasia. These severe complications could be attributed to the association of two factors: lower gestational age and lower use of ACs.

It is possible that the clinical characteristics of each group may explain these differences. The therapeutic labor, mainly due to the maternal hypertensive state, is often decided on after an in-depth evaluation and control of the maternal conditions, enabling a precious gain of several days, including the prescription of ACs and magnesium sulfate.

On the other hand, taking into account the causal factors of premature labor in the CG, the patients are often admitted in the advanced active phase, which prevents the adoption of preventative measures to reduce the postnatal risks.

The role of ACs appears to be increasingly decisive in reducing morbidity and, consequently, costs. An economic analysis of this issue[15] detected that among newborns weighing $< 1{,}500$ g, considering only the survivors, they were the group that most benefited from ACs, and that caused a significant reduction in all cost components, and a reduction of 36% in the total cost was achieved. This issue also appears to be reflected in the AHG, as ACs were not administered to 8.2% of the cases, a significant percentage that is a cause for concern.

In relation to hospital mortality, no significant differences were detected between the two groups, although the absolute risk of death in the CG was practically double that of the AHG. We should emphasize that there is a notable reduction in mortality rates in both groups when the birth weight reaches 750 g. These numbers may be important when facing critical clinical situations, in which bioethical dilemmas need to be resolved, assisting in the joint decision-making by the health team and the parents.

Our study did not identify different prognoses depending on the presence or absence of maternal AH. A Brazilian study that evaluated factors related to mortality and morbidity in very low birth weight newborns identified, as relevant risk factors, a gestational age of less than 30 weeks, the use of ACs, having a cesarean birth, being a male newborn, being an infant small for gestational age, the presence of respiratory discomfort syndrome, late sepsis, necrotizing enterocolitis, and the persistence of ductus arteriosus.[16] Based on these conditions, we can state that newborns in this weight category have more than 50.0% chance of dying, or surviving with definitive complications. Our results are close to this forecast, and do not enable the consideration of the presence of AH, particularly maternal preeclampsia, as a protective factor against in-hospital morbidity and mortality.

In relation to the outpatient follow-up of the survivors, a loss to follow-up of 14 newborns in the AHG (33.3%) and 11 newborns in the CG (34.4%) was reported. Our findings are higher than the 20.0% of loss to follow-up identified in a systematic review aimed at estimating risk factors for later complications and cognitive problems in newborns exposed to perinatal problems. This is an important aspect to consider, as it illustrates the difficulties in guaranteeing an effective follow-up for a special population of newborns in our country.

The evaluations of the ZS regarding the somatic growth in both groups did not identify any significant differences, showing a predominant distribution of values considered adequate for the age groups, although, in the control group, a higher number of children with scores lower than expected was identified.

The somatic development of children continues to depend on prenatal factors, such as the presence of maternal diseases or placental abnormalities and postnatal factors related to the release of the insulin-like growth hormone, access to nutrition, and the psychosocial environment. The results of this study do not enable us to affirm that the different processes related to prematurity influenced the somatic development of the children evaluated, even considering that hypertensive states lead to more placental problems, requiring fetal circulatory adaptation in the AHG.

On the other hand, the functional complications evaluated showed high rates in both groups, but without significant differences between them. One point to consider is the exclusive use of magnesium sulfate in the AHG, which did not result in any advantages for this group. Based on a systematic review published in 2009, we now have consistent evidence to recommend the routine use of magnesium sulfate in all premature births at between 24 and 34 weeks of gestation, aimed at reducing cerebral palsy in the second year of life.[17,18] It is assumed that the sample size included in this study did not have sufficient power to identify differences between the groups.

Loss to follow-up may affect the interpretation of the results among the survivors. Those with low complications

or mild limitations may be less willing to attend subsequent follow-up visits, assuming there would be no advantage to be gained from this evaluation, which may have led to an overestimation of the rate of complications in the newborns evaluated. On the other hand, children with severe complications have higher chances of death that would not be recorded, leading to an underestimation of the cases with better evolution. It should also be considered that our study is based in a reference hospital, which receives severe cases from various regions of the municipality, or even outside the state of São Paulo, which are limiting factors in terms of mobility for the newborns and their families.

As final considerations, our study identified significant rates of morbidity and mortality in both groups of VLBWIs. The difficulties of postnatal monitoring in both groups are highlighted, a factor that probably influenced the interpretation of the results for those who completed all the phases. It should also be taken into consideration that this first step of the evaluation does not mean that other problems, such as school performance and behavioral issues, may not be detected in future.

Our results refer to the presence of maternal AH, particularly preeclampsia. It should not be considered a protective factor in relation to the prognoses of premature newborn infants, as reported in a classic work on the subject.[19] We also observed that our finding is in line with a systematic review[20] that concluded that perinatal factors are less important than post-natal environmental factors in VLBWIs, and that follow-up strategies for these children are essential to reduce future damages.

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References

1 Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 2012;379(9832):2162–2172
2 –. Brasil. Ministério da Saúde. Informações de Saúde. DATASUS [Internet]. Nascidos vivos. 2013 [citado 2015 Nov 16]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinasc/cnv/nvuf.def
3 Passini R Jr, Cecatti JG, Lajos GJ, et al; Brazilian Multicentre Study on Preterm Birth study group. Brazilian multicentre study on preterm birth (EMIP): prevalence and factors associated with spontaneous preterm birth. PLoS One 2014;9(10):e109069
4 Horbar JD, Carpenter JH, Badger GJ, et al. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. Pediatrics 2012;129(06):1019–1026
5 Moreira RS, Magalhães LC, Alves CR. Effect of preterm birth on motor development, behavior, and school performance of school-age children: a systematic review. J Pediatr (Rio J) 2014;90(02):119–134
6 Rogvi RÁ, Forman JL, Greisen G. Prematurity, smallness-for-gestational age and later hospital admissions: a nation-wide registry study. Early Hum Dev 2015;91(05):299–306
7 Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33(03):130–137
8 de Oliveira LG, Karumanchi A, Sass N. [Preeclampsia: oxidative stress, inflammation and endothelial dysfunction]. Rev Bras Ginecol Obstet 2010;32(12):609–616
9 Pacagnella RC, Cecatti JG, Parpinelli MA, et al; Brazilian Network for the Surveillance of Severe Maternal Morbidity study group. Delays in receiving obstetric care and poor maternal outcomes: results from a national multicentre cross-sectional study. BMC Pregnancy Childbirth 2014;14:159
10 -. WHO child growth standards: lenght/height-for-age, weight-for-age, weigth-for-lenght, weight-for-height and body mass index-for-age: methods and development. Geneva: WHO; 2006
11 Frankenburg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of the Denver Developmental Screening Test. Pediatrics 1992;89(01):91–97
12 Ananth CV, Vintzileos AM. Maternal-fetal conditions necessitating a medical intervention resulting in preterm birth. Am J Obstet Gynecol 2006;195(06):1557–1563
13 Cavallo MC, Gugiatti A, Fattore G, Gerzeli S, Barbieri D, Zanini R; Neonatal Adequate Care for Quality of Life (NEO-ACQUA) Study Group. Cost of care and social consequences of very low birth weight infants without premature- related morbidities in Italy. Ital J Pediatr 2015;41:59–71
14 Mistry H, Dowie R, Franklin RC, Jani BR. Costs of neonatal care for low-birthweight babies in English hospitals. Acta Paediatr 2009;98(07):1123–1129
15 Ogata JF, Fonseca MC, Miyoshi MH, Almeida MF, Guinsburg R. Costs of hospitalization in preterm infants: impact of antenatal steroid therapy. J Pediatr (Rio J) 2016;92(01):24–31
16 Guinsburg R, de Almeida MF, de Castro JS, et al. Death or survival with major morbidity in VLBW infants born at Brazilian neonatal research network centers. J Matern Fetal Neonatal Med 2016;29(06):1005–1009
17 Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev 2009;(01):CD004661
18 Magee L, Sawchuck D, Synnes A, von Dadelszen P. SOGC Clinical Practice Guideline. Magnesium sulphate for fetal neuroprotection. J Obstet Gynaecol Can 2011;33(05):516–529
19 Schiff E, Friedman SA, Mercer BM, Sibai BM. Fetal lung maturity is not accelerated in preeclamptic pregnancies. Am J Obstet Gynecol 1993;169(05):1096–1101
20 Linsell L, Malouf R, Morris J, Kurinczuk JJ, Marlow N. Prognostic factors for poor cognitive development in children born very preterm or with very low birth weight: a systematic review. JAMA Pediatr 2015;169(12):1162–1172