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Rev Chil Pediatr. 2017;88(4):458-464
DOI: 10.4067/S0370-41062017000400003

ORIGINAL ARTICLE

Analysis of risk factors for neonatal death in Chile, 2010-2014

Análisis de los factores de riesgo de muerte neonatal en Chile, 2010-2014

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Received: 26-7-2016; Accepted: 26-12-2016

Abstract

Aim: To analyze socio-demographic as maternal and newborn factors associated with neonatal mortality in a tertiary hospital in Chile. **Patients and Method:** A retrospective analysis of case (neonatal death) and control (live births) was performed. A match 1:2 proportion considering year, month of birth and gender was made. By reviewing medical records and existing databases, we analyzed socio-demographic and pathophysiological variables of the mother and their newborn in a period between 2010 and 2014. **Results:** During the period of study 81 neonatal deaths occurred in the hospital, with an estimated rate of 5.8 per thousand live births. Sixty-five cases were recruted, who were compared with 130 controls. The main causes of death were prematurity and congenital malformations. It was found that the presence of preterm birth (OR: 3; 95% CI 1.1-8.7), newborn small for gestational age (OR: 4; 95% CI 1.7-12.1) Apgar score at minute 4-7 (OR: 4; 95% CI 1.8-10.5), maternal activity outside the household (OR: 4; 95% CI 2.3-8.7), and cesarean delivery (OR: 3; 95% CI 1.5-5.6) were the most prevalent risk factors. **Conclusion:** Neonatal mortality is associated with prematurity. Therefore it is of relevance to continue promoting efforts to prevent preterm birth.

Keywords:
Neonatal mortality, referral hospital, prematurity, Chile

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Introduction

Health indicators of mothers and children are essential, because they reflect the standard of living and the state of development and progress of a country. According to the Statistics and Research in Health Directorate[1] in 2012, Chile stands out for having an infant mortality rate of 7.4 per 1000 live births, the lowest rate in South America[2]. However, despite that reaching an infant mortality rate of 5.3 per 1000 live birth[3] is one of the Millennium Development Goals established by the United Nations (UN), Chile has not been able to go down to less than 7 per 1000 live births in the last 5 years[1].

Neonatal death is defined as a fatal even during the first 28 days of life, which constitutes a 72% of all infant deaths according to the Chilean Department of Statistics and Health Information (DEIS)[1]. At a country level, these rates of neonatal mortality are not uniform. For example, the highest rate of neonatal mortality are found in Arica and Parinacota and in Los Lagos Regions[1].

The highest period of fatal risk in the first year of life is the neonatal stage[4]. Neonatal death is a multifactorial event. According the World Health Organization (WHO), the leading causes of newborn deaths worldwide are: premature birth and low birth weight, infections, asphyxia and birth trauma. These causes explain an 80% of deaths in this age group[5]. In Chile, it has been concluded that the main causes of neonatal death are congenital malformations, chromosomal abnormalities, prematurity and neonatal sepsis[4]. In addition, evidence suggests an association between increased risk of neaonatal death and maternal factors (directly or indirectly linked), such as: age[6], low level of education[7], obesity in pregnancy[8], hypertension and diabetes[9,10], as well as with social factors such as marital status and other socioeconomic variables[11,12]. Neonatal death is also associated with factors related to healthcare during pregnancy and childbirth, such as insufficient prenatal control and cesarean delivery[13,14].

Since the Hospital of Chillán is a reference hospital in the Bio Bio Region, this study seeks to identify local risk factors associated with neonatal mortality between 2010 and 2014.

Patients and Methods

This is a retrospective study, including neonatal death (cases) and comparing them to live infants (controls), approved by the Scientific Ethical Committee of Herminda Martin de Chillán Clinical Hospital (ORD No. 548 dated 08/28/2010). Clinical data and secondary databases were consulted, requesting information from the hospital's statistics unit and the Ñuble Health Service. All information was tabulated and harmonized using a database especially designed for the study.

The study comprehends the total number of live newborns at the Herminda Martin Clinical Hospital during the analysis period. The inclusion criteria for the cases were: birth in the hospital, gestational age at birth greater than 22 weeks or equal, birth weight equal or greater than 500 grams, death occurred in the hospital within the first 28 days of life.

The selection of controls was performed by simple random sampling from the statistical database of births. Two controls were selected for each case, matched by place, year, month of birth and gender. For those cases of deceased newborns whose gender was undetermined, their controls were randomly chosen without regard to the gender of the newborn. Those infants who were not able to find complete information (out-of-hospital deliveries and when the clinical records were not found) were excluded from the study.

The neonatal mortality was taking into account as a dependent variable, thus, 21 different study variables were divided into neonatal, maternal and childbirth variables (see Table 1). We present in this analysis those variables of exposure that were presented in more than three cases in any of the groups under study.

A descriptive analysis of the variables was made, in which the quantitative variables were expressed in means and standard deviations, while the qualitative variables were expressed as a percentage of the study group. To establish differences between clinical cases

Table 1. Summary of variables

	Variable
Newborn's physiopathologic characteristics	• Neonatal death (dependent variable) • Gestational age • Neonatal weight • Relationship weight to gestational age • Sepsis • Apgar score • Congenital malformation • Prenatal diagnostic of malformation • Premature
Maternal factors: Socio demographics and physiopathologic	• Age • Education • Marital status • Nutritional status at delivery • Occupation • Previous perinatal death • Diagnosis of hypertension • Diagnosis of diabetes
Factors related with prenatal control and delivery	• Prenatal control • Vaginal delivery or cesarean section • Premature delivery • Etiology of premature delivery

and controls, the bivariate analysis was performed using the t-student test, in order to compare means between groups. Regarding qualitative variables, the Chi-square test was used, with a confidence interval of 95%. Odds ratio (OR) was calculated by binary logistic regression analysis for each risk factor significantly associated with neonatal death in the bivariate analysis. For the analysis of adjusted OR, all premature infants (birth before 32 weeks of gestation), those with an Apgar score less than 3 points and congenital malformations not compatible with life were excluded in every model. The adjustment variables were chosen according to previous reports in the literature. The interaction between adjustment variables was not evaluated. A Kaplan-Meier analysis was performed considering the child survival probability, global or associated with preterm (< 37 weeks and/or spontaneous). The comparison between the two groups was performed using the Mantel-Cox test. Statistical analysis was performed using SPSS 21 version and Graph Pad Prism 6.0 version.

Results

According to the information provided by the Statistical Unit of the Herminda Martin Clinical Hospital, a total of 81 neonatal deaths occurred during the period between 2010 and 2014. The estimated neonatal death rate in the hospital was 5.8 per 1000 live births. From these neonatal deaths, we reviewed 65 cases that met the inclusion criteria (which represent 80% of deaths occurred in the hospital). From them, 74% died within the first 7 days of their life. This group was compared to 130 live births.

The main causes of death, according to medical records, were prematurity (57%) and congenital malformations (29%). Main characteristics of newborns are shown in Table 2. Mean pediatric age and birth weight were lower in the group of infants who died than those in the control group ($p < 0.0001$, in both cases). In both groups, a higher proportion of newborns adequate for gestational age were observed, 60% in the cases group and 82% in the control group. However, a higher proportion of small-for-gestational-age infants (SGA) were found in the control group (32% vs 8%, $p < 0.0001$).

There was a major presence of congenital malformations (37% vs 3%) and sepsis (32% vs 0%) being greater in cases than controls. The Apgar score was lower (66% and 44%, respectively) in the group of deceased infants at one minute or at five minutes than in the control group.

Table 2. Newborn's characteristics

Characteristic	Cases	Controls	p
Infant age, wks ± ds (n)	29.0 ± 5.7 (65)	38.5 ± 2.1 (129)	< 0.0001
Weight, g ± sd (n)	1.292.5 ± 966.2 (65)	3.332.4 ± 627.5 (130)	< 0.0001
Relationship weight to gestational age			
SGA, % (n)	32 (21)	8 (10)	< 0.0001
AGA, % (n)	60 (39)	82 (106)	
LGA % (n)	8 (5)	10 (14)	NS
Sepsis			
Yes, % (n)	32 (21)	0 (0)	< 0.0001
No, % (n)	68 (44)	100 (130)	
Apgar score			
1 min (mean ± sd)	3.7 ± 2.7 (65)	8.7 ± 1.0 (129)	< 0.0001
5 min (mean ± sd)	5.2 ± 2.9 (65)	9.4 ± 0.6 (129)	< 0.0001
Congenital malformation			
Yes, % (n)	37 (24)	3 (4)	< 0.0001
No, % (n)	63 (41)	97 (126)	
Antenatal Diagnostic of CMF			
Yes, % (n)	75 (18)	75 (3)	NS
No, % (n)	25 (6)	25 (1)	

Values expressed as mean ± standard deviation (sd). SGA, small for gestational age; AGA, adequate for gestational age; LGA, large for gestational age; CMF, congenital malformation. NS, not significant.

Maternal characteristics are described in Table 3. There was a higher percentage of mothers who were still students or mothers who work outside their home in the group of cases than controls (71% vs 38%, p = 0.0001). In addition, the history of perinatal death was higher in mothers whose newborns died (8% vs 1%). No differences were found in the history of diabetes or hypertension in the group of mothers studied.

Regarding the factors related to the healthcare during pregnancy and childbirth (Table 4), it was found that the number of prenatal controls was higher in the control group compared to the clinical cases. Regarding the way of delivery, a greater percentage of the newborns who died were born via cesarean section compared to the control group (60% vs 31%, respectively, p < 0.0001). A higher percentage of preterm birth was observed in the group of newborns who died compared to the control group (83% vs 8%, respectively, p < 0.0001). Within this diagnosis, spontaneous preterm birth was the most frequent in the group of neonates who died (70 vs 54%, p = 0.01). A 50% of the deceased newborns died at day 2 (95% CI: 1-3). Similarly, children who died due to prematurity and spontaneous preterm delivery were analyzed, as shown in the analysis of Kaplan Meier (Figure 1).

Table 5 includes crude and adjusted OR for factors associated with neonatal death. According to adjusted ORs, the risk of death increases 3-fold in preterm infants older than 32 weeks of gestation, compared with babies delivered at term (p < 0.02). According to the weight-for-gestational age relationship, SGA infants have a 4-fold greater risk of death than controls (p < 0.002). While the Apgar score between 4 and 7 per minute of life was also found to be a statistically significant risk factor for neonatal death (adjusted OR = 4.4 95% CI = 1.8-10.5, p = 0.001).

Regarding maternal factors, it was found that performing an activity outside their home was associated with at least 4 times the risk of neonatal death com-

Table 3. Maternal characteristics

Characteristic	Cases	Controls	p
Age, years ± sd (n)	27.6 ± 7.5 (65)	25.9 ± 6.3 (130)	NS
Education, years ± sd (n)	10.7 ± 2.6 (65)	10.8 ± 2.5 (130)	NS
Marital status:			
Single, % (n)	31 (20)	45 (58)	NS
Married/Cohabiting, % (n)	69 (44)	55 (72)	
Occupation			
Housewife, % (n)	29 (19)	62 (81)	
Out of home % (n)	71 (46)	38 (49)	0.0001
Nutritional status			
Low weight, % (n)	7 (4)	13 (16)	NS
Normal, % (n)	17 (10)	19 (24)	
Overweight, % (n)	22 (13)	10 (13)	NS
Obese, % (n)	54 (31)	58 (72)	NS
Hypertension			
Yes, % (n)	14 (9)	11 (14)	NS
No, % (n)	86 (56)	89 (116)	
Diabetes			
Yes, % (n)	5 (3)	13 (17)	NS
No, % (n)	95 (62)	87 (113)	

Values expressed as mean ± standard deviation (sd). NS, not significant.

Table 4. Factors related with prenatal control and delivery

Characteristic	Cases	Controls	p
Prenatal Control:			
No control during pregnancy, % (n)	6 (4)	1 (1)	NS
Prenatal control attendance, % (n)	94 (58)	99 (129)	
GA at initial control (wks ± sd)	10.8 ± 4.7 (55)	11.9 ± 5.6 (125)	NS
Total number of controls (mean ± sd)	7.2 ± 4.4 (52)	10.1 ± 3.6 (125)	0.0001
Delivery			
Vaginal, % (n)	40 (26)	69 (90)	< 0. 0001
Cesarean, % (n)	60 (39)	31 (40)	
Prematurity			
Yes, % (n)	83 (54)	8 (11)	< 0.0001
No, % (n)	17 (11)	92 (119)	
Delivery of premature			
Spontaneous, PRM % (n)	70 (38)	54 (6)	0.01
Interruption, % (n)	30 (16)	46 (5)	

Values expressed as average ± standard deviation (sd). GA, gestational age. PRM, premature rupture membranes. NS, not significant

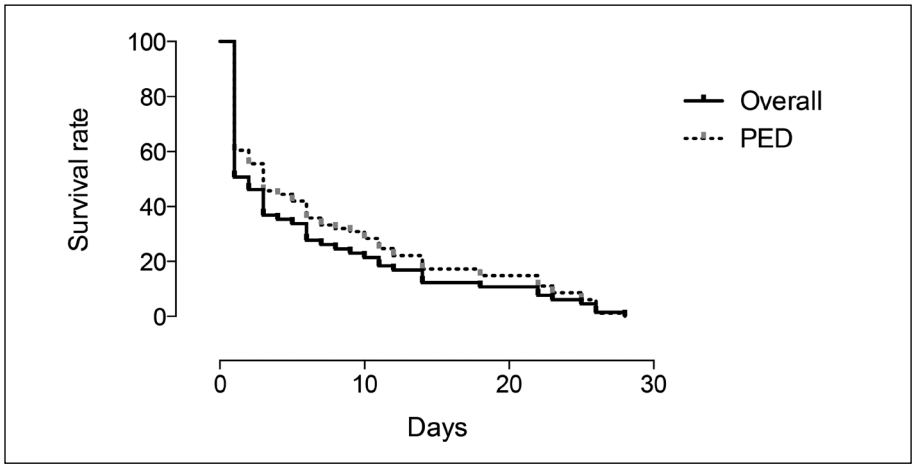

Figure 1. Survival rate associated to prematurity and premature spontaneous delivery (PED). It is shown neonatal survival in the total sample (Overall) or associated with premature delivery (< 37 weeks and/or premature spontaneous delivery). Premature delivery was present in most of the cases.

Table 5. Odd ratio (OR) crude and adjusted for neonatal death risk factors

	Crude			Adjusted		
Factor	OR	95% IC	p	OR	95% IC	p
Premature delivery > 32 wks	2.4	0.89 - 6.6	0.08	3.1	1.1 - 8.7	0.02
SGA	5.7	2.4 - 13.1	< 0.001	4.6	1.7 - 12.1	0.002
Asphyxia (moderated depression)	4.9	2.1 - 11	< 0.001	4.4	1.8 - 10.5	0.001
Maternal activity outside home	4.4	2.3 - 8.4	< 0.001	4.5	2.3 - 8.7	< 0.001
Cesarean section	3.3	1.8 - 5.9	< 0.001	3	1.5 - 5.6	< 0.001

SGA, small for gestational age. Premature delivery adjusted by maternal age, maternal body mass index at delivery, prenatal control attendance. SGA adjusted by maternal age, hypertension, presence of congenital malformation. Asphyxia adjusted by cesarean section, maternal age. Maternal activity adjusted by years of formal education, single mother. Cesarean section adjusted by hypertension, diabetes, maternal age.

pared to the control group (adjusted OR = 4.5, 95% CI = 2.3-8 , 7, p = 0.001). Finally, cesarean delivery was associated with a 3-fold increase in the risk of death (p < 0.001) (Table 5).

Discussion

Among the risk factors found in this study, prematurity was the leading causes of neonatal death at Chillán Hospital. These results agree with national and international studies[15,16]. In addition, asphyxia, congenital malformations, hyaline membrane and sepsis were found as factors associated with neonatal death, confirming also what has been reported in the literature[17]. Congenital malformations are present in this study in a 37% of the deceased cases, lower than what had been published[18], where indicates that malformations are present in 45% of newborns who died in our country. The causes for this clear difference were not studied. However, it may be related to different rates of neonatal mortality associated with malformations found in Chilean hospitals[18].

Regarding other neonatal risk factors, including the mother and the delivery care, we find some peculiarities in our study. For example, the literature has reported that maternal age[6], marital status[11], lower level of education[7], presence of hypertension or diabetes[9,10] and maternal obesity[8,19] are risk factors for neonatal death, which we could not be proved in our research.

Regarding pregnancy and delivery care, only significant differences were found in the way of delivery, being the cesarean rate the highest in the group of neonates who died. This rate was 60%, which is the double of what has been reported at national level[14]. Causes for these differences were not analyzed in this study. However, indirectly this could represent a greater morbidity, both maternal and fetal in the group of deceased before childbirth.

According to the prematurity rate, the number of prenatal controls was lower in mothers with deceased newborns. However, it is considered that the national legislation indicates that every pregnant woman should have prenatal care. It is interesting to notice that this was not observed in any of the two groups analyzed (neonatal deaths and controls). Moreover, a lower percentage of cases of neonatal death were very close to this regulation (94% and 99% of clinical cases and controls, respectively). We recommend enhance all efforts focused on improving early recruitment and the corresponding monitoring of pregnant women.

Adjusted logistic regression analysis showed that preterm birth, SGA, low Apgar scores, mothers with out-of-home activities and cesarean births were 3 to 5 times more frequent in children with neonatal death compared to the control group. Among them, the main risk factor reported in the literature[15,17] and found in this study was premature delivery. Therefore, it is necessary to continue reinforcing all efforts to prevent this type of pathological delivery. We should remember that the origin of most premature births was spontaneous or ruptured membranes, so it would be interesting to review compliance with the protocol of care for preterm delivery, at all three levels of care.

Another finding in this research was that a 25% of mothers who had a spontaneous preterm birth were admitted in the hospital in labor or even at delivery (data not shown).

We are aware that there are several limitations in this study. Even it is a retrospective analysis, we included 80% of the total number of neonatal deaths occurring in the hospital, and analyzed both the maternal chart and the neonatal records. Moreover, a control group was included to perform comparative statistics. It was not possible to find statistical significance in those "classic" risk factors of neonatal death. However, despite the complete review of the clinical file, it is not possible to rule out underreporting of the diagnoses, especially in those cases of comorbidity.

In conclusion, neonatal death was associated with premature delivery, in one of the reference hospitals of the Bio Bio Region, Chile.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

Fondecyt Regular 1140586, Fondequip EQM140104, DIUBB GI153109/EF and GI 152920/EF.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Acknowledgements

We thank all the Gynecology and Obstetrics Service staff, as well as the Department of Statistics belong to Hospital Clinico Herminda Martin for their valuable help in collecting this information. In addition, we thank Dr. Luisa Zipper from the Servicio de Salud Ñuble for providing us the databases of the cases reported and all suggestions given for the development of this study. To the professors Jaqueline Araneda and Patricio Oliva from the Master's Program in Public Health of the Universidad del Bio Bio for their continuous training work. This study was funded by the FONDECYT project 1140586.

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