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Determinants of neonatal survival among newborns who died between 2014 and 2017 in Ecuador: A study analyzing national databases.

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Abstract

Introduction: Neonatal mortality is an indicator in public health. In Ecuador, the neonatal death rate is 6 per 1,000 live births. The objective of this study was to identify the main determinants of neonatal mortality in newborns who died between 2014 and 2017 in Ecuador.

Methodology: This study is an analysis of the national database of the National Institute of Statistics and Censuses of Ecuador-INEC and the Ministry of Public Health of Ecuador, which records the mortality of newborns who died between 2014 and 2017. Prenatal variables were evaluated, natal, postnatal and sociodemographic conditions and their association with mortality, measured in days of survival. Adjusted hazard ratios for neonatal death (Hazard Ratio [HR]) were estimated using Cox proportional hazards models and inverse probability-weighted Cox regression.

Results: A total of 2893 newborns were included in the study, 1380 (48%) were female; median gestational age (P25 to P75) at birth: 31 (27 to 36) weeks. The median survival time in days of life was significantly longer for each increase in Apgar score at 5 minutes: 0.2 days for ≤ 4 points, 2 days for 5 points 2.9 days for 6 points, 3.1 days for 7 points, 3.8 days for 8 points, 4.4 days for 9 points, and 5.5 days for 10 points. After adjusting for prenatal, natal, postnatal, and sociodemographic variables, the HR was 32% (95% CI: 27% to 37%) higher for each two - to three-point decrease in Apgar (P < 0.01).

Conclusions: The APGAR assessment at 5 minutes predicts the survival of the newborns, the higher values are associated with more survival. The factors that increase the risk of mortality are adolescent and elderly maternal age, extreme premature gestational age, extreme low weight, the presence of malformations and neonatal asphyxia. The sociodemographic factors were births in first level institutions and newborns born in zone 3 of Ecuador (Cotopaxi, Tungurahua, Chimborazo and Pastaza).

Keywords:
MESH: Infant, Newborn; Neonatology; Infant Mortality; Early Neonatal Mortality; Risk Factors.

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Introduction

Neonatal death is defined as death produced from birth to 28 days of life; in addition to being a public health problem, it is a health indicator at the population level [1].

According to figures established by the World Health Organization (WHO), in 2019, 2.4 million children died before their first month. Approximately 6,700 newborns die daily, representing 47% of deaths in children under 5 years of age [2].

The average infant mortality in Latin America is approximately 15.7 deaths per thousand live births (ptlv), being lower in countries such as Cuba and Chile <7 ptlv and higher in Guyana, Bolivia, and especially Haiti, with rates of 26.28 and 54 ptlv, respectively [3]. This is associated with various factors, such as high fertility, high poverty rates, and low health coverage [4].

In Ecuador, the infant mortality rate in 2019 was ptlv 6 [5], and in 2020, the rate decreased to 4.6 ptlv [6].

The leading causes of neonatal death are reported as intrauterine hypoxia 33.7%, placental abruption or hemorrhage that has affected the fetus in 3.9%, maternal hypertensive disorders that have affected the fetus in 2.4%, extreme prematurity in 1.1%, morphological abnormalities and functional of the placenta in 0.9%, oligohydramnios in 0.8%, syndrome of the newborn of a mother with gestational diabetes in 0.6% and premature rupture of membranes in 0.6%; a high percentage of 45.2% the cause is not specified [6].

Among the main determinants of prenatal health that influence neonatal complications are inadequate placental fetal assessment, maternal history of gestational diseases, lack of attendance at prenatal controls, use of harmful substances during pregnancy, and poor nutrition.

Another factor is extreme maternal age; the risk of neonatal mortality is markedly higher in mothers younger than 16 [7] or older than 35 years. Likewise, a higher probability of adverse outcomes has been observed among mothers with parity ≥ 3 children [8].

On the other hand, the main natal determinants that increase the risk of neonatal mortality are gestational age, birth weight, the presence of hypoglycemia, and hyperbilirubinemia; for example, preterm infants and infants incredibly very small for gestational age are more vulnerable than term infants to birth trauma, neurological and soft tissue damage, and traumatic intracranial hemorrhage [9].

Additionally, the type of delivery could be a risk factor in some cases; for example, there is an association between elective cesarean section and increased neonatal respiratory morbidity and lacerations and a 1.5 times higher risk of neonatal mortality after both planned, unplanned cesarean sections. Designed, compared with vaginal birth [10].

In the postnatal period, unidentified and untreated diseases contribute to neonatal mortality [11].

In general, any prenatal, natal, or postnatal factor can have an impact on neonatal morbidity and mortality; one study found that factors associated with increased risk of neonatal ICU admission included high multiparity (adjusted OR 1.46), gestational diabetes (adjusted OR 1.92), prolonged rupture of membranes (revised OR 5), fetal distress (adjusted OR 1.84), prematurity (adjusted OR 43.78), low birth weight (adjusted OR 42), high-order multiple gestations (adjusted OR 9.58), and low Apgar score at 5 min (modified OR 10) [12].

Several studies have determined that different social and economic factors are related to the increased risk of neonatal death, such as low maternal education, home delivery without a qualified provider, delay in seeking medical attention, lack of preparation of families, harmful cultural practices, poorly trained care providers, adverse economic situation, social exclusion, maternal illiteracy, negative attitudes of parents and relatives, gender bias, inability to pay for care and lack of prenatal services, basic natal and postnatal [14-18].

This study identifies the main factors affecting Ecuador's neonatal health.

Population and methods

Design of the investigation

The present study is an analytical and retrospective observational database analysis.

Stage

The unit of analysis of this study corresponds to the information obtained from the National Medical Surveillance System (SVMN) of the Ministry of Public

Health of Ecuador. The study period was from January 1, 2014, to December 31, 2017.

Participants

Records of newborns with deaths occurring in public or private fields with a history of survival in days were included. Incomplete forms and those without Apgar scores at 5 minutes were excluded.

Universe and sample

The sample calculation was a nonprobabilistic census type since all the records of the study period were included.

Variables

The dependent variable was the Apgar score at 5 minutes. Independent variables were recorded: demographics of the mother and the newborn and comorbidities.

Data/Measurement Sources

The source is the national database. A validated and mandatory national reporting base for all public and private medical centers in Ecuador. The national regulatory authority provided the database for research purposes devoid of specific identification data in Excel format. To fill in the data, the regulatory authority published the corresponding regulations in the official registry to maintain the data quality with information losses of less than 10%.

Statistical method

In the first part of the study, a statistical description of the variables is made. Average and standard deviation are used for variables on a regular distribution scale, median with interquartile range for variables on a scale with nonparametric distribution, and frequencies with percentages for categorical variables. A multivariate study was performed using the Apgar test at 5 minutes in the second part of the study. The sample was divided into 4 groups: group 1 Apgar at 5 minutes ≤ 4 points, group 2 Apgar at 5 minutes between 5 and 6 points, group 3 Apgar at 5 minutes between 7 and 8 points, and group 4 Apgar at 5 minutes between 9 and 10. Analysis of variance was used to compare means, and Kruskal–Wallis was used to compare categorical variables between groups. A survival study with Cox regression is presented, for which the hazard ratio is used to measure the association between risk factors and mortality over time. Kaplan–Meier graphs are shown to represent survival in the groups analyzed. The statistical program used was SPSS V 22.0 (Armonk, IBM).

Results

Participants

A total of 2,893 neonatal records entered the study (Figure 1), representing a loss of information of 9.3%.

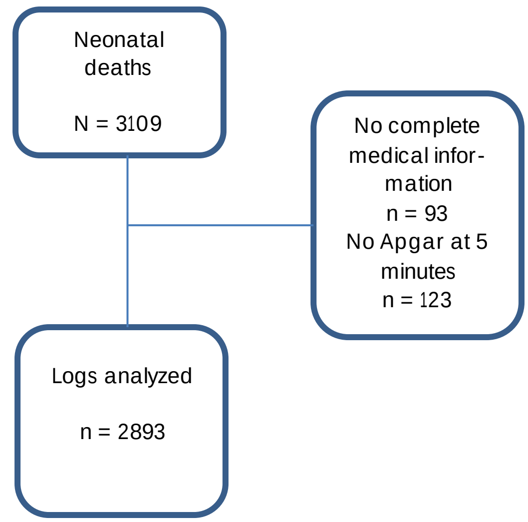

Figure 1. Chart of registered infants included and excluded from the study.

Sample Characteristics

A total of 2893 neonates were included; 1380 (48%) were female, the median gestational age was 31 weeks (P25 to P75: 27 to 36), and the mean birth weight was 1651 ± 922 grams. Fifty-nine percent were born by cesarean section, with a median Apgar at 5 minutes of 6 (P25 to P75: 4 to 8). Deaths in third-level health institutions were 53.89%, in second-level institutions were 43.93%, and in the first level were 2.18%. By geographical area in Ecuador, the majority belonged to Zone 3 (Cotopaxi, Tungurahua, Chimborazo, and Pastaza: 492 (17%), followed by Zone 8: (13%) Figure 2).

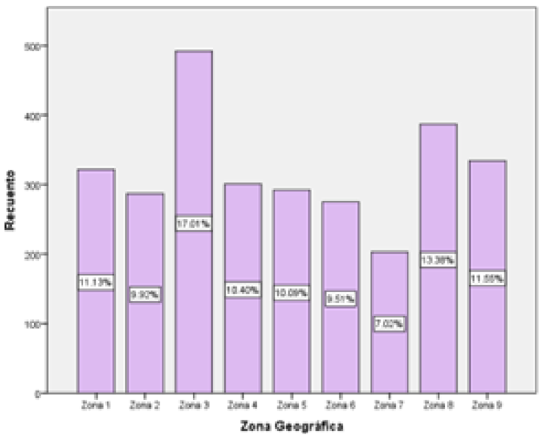

Figure 2. Distribution of frequencies according to geographical area.

Zone 1: Esmeraldas, Imbabura, Carchi, Sucumbíos
Zone 2: Pichincha, Napo, Orellana
Zone 3: Cotopaxi, Tungurahua, Chimborazo, Pastaza
Zone 4: Manabí, Santo Domingo de los Tsáchilas
Zone 5: Santa Elena, Guayas, Bolívar, Ríos, Galapagos
Zone 6: Canar, Azuay, Morona Santiago
Zone 7: El Oro, Loja, Zamora Chinchipe
Zone 8: Guayaquil, Samborondón, Duran
Zone 9: Metropolitan District of Quito

The mean maternal age was 26.4 ± 7.2 years; 1,655 (57%) were nulliparous, and 1,739 (60%) patients had <4 prenatal controls. Regarding comorbidities, congenital malformations (53.96%) were the most frequent, followed by disorders related to asphyxia (24.02%) and infectious diseases (18.42%); there were 3.59% of previously unclassified disorders.

Multivariate analysis

The median survival time in days of life was significantly longer for each increase in Apgar score at 5 minutes; in group 1 (G1) with Apgar ≤ 4 points, it was 0.2 days; in group 2 (G2) with Apgar from 5 to 6, it was 2.5 days; in group 3 (G3) with Apgar from 7 to 8, it was 3.5 days; and in group 4 (G4) with Apgar from 9 to 10, it was 5.1 days (Table 1). There was a relationship between greater prenatal control and higher Apgar scores; the same occurred with gestational age and birth weight.

There was an inverse relationship between Apgar, asphyxia, and neonatal malformations (Table 1).

Table 1. Prenatal, natal, postnatal, and sociodemographic variables according to the Apgar scale score at 5 min.

Variables	Apgar scored at 5 minutes (2893)				*P*
	Group 1 Apgar ≤ 4 (n = 763)	**Group 2** Apgar 5 and 6 (n = 719)	**Group number 3** Apgar 7 and 8 (n = 864)	**Group 4** Apgar 9 and 10 (n = 547)	
Neonatal survival (days; P25, P75)	0.2 (<0.1 to 2)	2.5 (1 to 7)	3.5 (1.4 to 10.5)	5.1 (2.3 to 13.5)	<0.01
PRENATAL FACTORS					
Maternal age (years; mean, SD)	21.3 ±5.6	29.8±10.1	26.7 ±4.3	27.4 ± 8.5	<0.01
Parity					
Nullipara (n, %)	482 (63)	489 (68)	423 (49)	261 (48)	0.01
Multiparous (n, %)	281 (37)	230 (32)	441 (51)	286 (52)	0.01
Prenatal checkups					
< 4 (n, %)	628 (82)	525 (73)	412 (48)	174 (32)	<0.01
≥ 8 (n, %)	135 (18)	194 (27)	452 (52)	373 (68)	<0.01
Sex					
Female (n, %)	392 (51)	342 (48)	417 (48)	424 (77)	0.05
Male (n, %)	411 (49)	377 (52)	447 (52)	123 (23)	0.05
Gestational age (weeks; median, P25 to P75)	29 (25 to 34)	31 (27 to 35)	32 (29 to 36)	34 (30 to 37)	<0.01
BIRTH FACTORS					
birth weight (gr; mean, SD)	1452 (964)	1500 (859)	1652 (818)	2281 (903)	<0.01
Type of delivery					
Cesarean section (n, %)	449 (59)	214 (30)	518 (60)	286 (52)	<0.01
Eutocic (n, %)	252 (33)	245 (34)	293 (34)	233 (43)	<0.01
Dystocic (n, %)	56 (7)	260 (36)	53 (6)	28 (5)	<0.01
POSTNATAL FACTORS					
Comorbidities					
Asphyxiation (n, %)	222 (29)	184 (26)	203 (23)	86 (16)	<0.01
Malformations (n, %)	454 (60)	412 (57)	443 (51)	252 (46)	<0.01
Infections (n, %)	63 (8)	109 (15)	185 (21)	176 (32)	<0.01
Unclassified (n, %)	24 (3)	14 (2)	33 (5)	33 (6)	<0.01
SOCIODEMOGRAPHIC FACTORS					
Type of health care					
Public (n, %)	476 (62)	438 (61)	689 (80)	517 (95)	<0.01
Private (n, %)	287 (38)	281 (39)	175 (20)	30 (5)	<0.01
Level of health care					
I level (n, %)	19 (2)	14 (2)	16 (2)	14 (3)	<0.01
II level (n, %)	289 (38)	267 (37)	417 (48)	298 (54)	<0.01
III level (n, %)	455 (60)	438 (61)	431 (50)	235 (43)	<0.01
Geographical area					
1 (n, %)	93 (12)	87 (12)	76 (9)	66 (12)	<0.01
2 (n, %)	130 (17)	98 (14)	44 (5)	15 (3)	<0.01
3 (n, %)	249 (33)	198 (28)	31 (4)	14 (2)	<0.01
4 (n, %)	77 (10)	81 (11)	89 (10)	54 (10)	<0.01
5 (n, %)	89 (11)	120 (17)	67 (7)	16 (3)	<0.01
6 (n, %)	15 (2)	15 (2)	143 (17)	102 (19)	<0.01
7 (n, %)	30 (4)	14 (1)	95 (11)	64 (12)	<0.01
8 (n, %)	45 (6)	70 (10)	162 (19)	110 (20)	<0.01
9 (n, %)	35 (5)	36 (5)	157 (18)	106 (19)	<0.01

Variables were made using Chi^2, ANOVA, and Kruskal–Wallis. The geographic area is the caption of figure 2.

COX Proportional Hazards Analysis

Regarding the multivariate modeling of Cox proportional hazards, after adjusting the different variables and considering an Apgar score of 9 to 10 points as a reference, the adjusted HR was 32% (95% CI: 27-37) higher for each decrease in Apgar score at 5 minutes from two to four points (P < 0.01) (Table 2).

A similar increase in HR was found for each decrease in the Apgar category when the analysis was stratified across gestational age categories at birth, as follows: 41% (95% CI: 35-48, *P* < 0.01) increased when infants were highly preterm, 39% (95% CI: 25-54, P < 0.01) increased for moderately preterm infants, and 24% (95% CI: 14-34, *P* < 0.01) increased when newborns were full term; for postterm infants (n = 56), although not significant (*P* = 0.97), HR was higher in most strata compared with better Apgar scores (9 to 10) at 5 minutes (Table 2).

When performing inverse probability-weighted proportional hazards (IPW Cox) models after an artificial cutoff at 21 days of follow-up, the adjusted survival estimates yielded very similar results, corroborating a "dose–response" form of association between Apgar score and survival time in days of life. Both in the complete sample and the one stratified by categories of gestational age at birth (Table 3 and Figure 2).

Table 2. Hazard ratios (HR) and HR adjusted for Apgar score at 5 minutes from two to four points.

Variables	Adjusted HR (95% CI)	*P*
PRENATAL FACTORS		
Maternal age (optimal age - reference)		
teen pregnancy	1.41 (1.36 to 1.50)	<0.01
elderly mother	1.33 (1.21 to 1.47)	<0.01
Parity (Nulliparous - reference)		
Multiparous	0.86 (0.72 to 0.90)	0.01
Prenatal controls (< 4 - reference)		
Greater than or equal to 8	1.02 (0.91 to 1.14)	0.01
Sex (male - reference)		
Female	1.06 (0.98 to 1.14)	0.13
Gestational age (Extreme preterm - reference)		
moderate preterm	0.83 (0.73 to 0.95)	<0.01
full term	0.77 (0.60 to 0.99)	0.04
postterm	0.88 (0.62 to 1.23)	0.44
BIRTH FACTORS		
Birth weight (Underweight extreme - reference)		
extreme low weight	0.85 (0.74 to 0.98)	0.02
very low weight	0.82 (0.70 to 0.96)	0.01
Low weight	0.83 (0.68 to 1.00)	0.05
suitable weight	0.89 (0.71 to 1.13)	0.34
macrosomic	0.78 (0.49 to 1.27)	0.31
Type of delivery (Cesarean section - reference)		
eutocic	1.06 (0.97 to 1.16)	0.18
dystocia	1.15 (0.96 to 1.37)	0.13
POSTNATAL FACTORS		
Apgar at 5 minutes (Apgar 9 - 10 Reference)		
Average (7 and 8)	1.26 (1.12 to 1.42)	<0.01
Moderate initial depression (5 and 6)	1.48 (1.29 to 1.68)	<0.01
Initial moderate depression (3 and 4)	1.99 (1.70 to 2.34)	<0.01
Severe initial depression (0, 1, 2)	3.33 (2.84 to 3.90)	<0.01
Comorbidities (Asphyxia - Reference)		
Malformations	0.98 (0.94 to 1.18)	0.26
infections	0.60 (0.53 to 0.69)	<0.01
Disorders not previously classified	0.83 (0.66 to 1.04)	0.11
SOCIODEMOGRAPHICS FACTORS		
Type of health care (Private - reference)		
public	1.20 (1.07 to 1.34)	<0.01
Level of health care (First level - reference)		
Second level	0.69 (0.51 to 0.93)	<0.01
Third level	0.65 (0.48 to 0.87)	<0.01
Geographic numerical zone (Zone 1 –reference)		
Zone 2	1.08 (1.00 to 1.24)	<0.01
zone 3	1.18 (1.07 to 1.32)	<0.01
Zone 4	0.77 (0.58 to 0.88)	0.01
Zone 5	0.65 (0.54 to 0.86)	0.01
zone 6	0.91 (0.70 to 1.03)	0.12
Zone 7	0.98 (0.80 to 1.15)	0.13
Zone 8	0.75 (0.61 to 0.90)	<0.01
Zone 9	0.78 (0.64 to 0.96)	<0.01

Variables were made using Chi^2, ANOVA, and Kruskal–Wallis. The geographic area is the caption of figure 2.

Table 3. Adjusted hazard ratios (95% CI) by gestational age category a

Apgar at 5 minutes	Prematureex-treme n = 1790	*P*	Pretermmoderate n = 412	*P*	full term n = 635	*P*	Post-term n = 56	*P*
Standard (9 and 10) (ref.)	1	-	1	-	1	-	1	-
Normal (7 and 8)	1.27 (1.07 -1.52)	<0.01	1.26 (0.95 - 1.67)	0.11	1.36 (1.08 - 1.71)	<0.01	1.68 (0.50 - 5.66)	0.40
Moderate initial depression (5 and 6)	1.51 (1.26 -1.83)	<0.01	1.55 (1.10 - 2.19)	0.01	1.74 (1.33 - 2.28)	<0.01	3.02 (0.46 - 19.85)	0.25
Initial moderate depression (3 and 4)	2.35 (1.88 - 2.96)	<0.01	1.82 (1.22 - 2.71)	<0.01	1.77 (1.25 - 2.51)	<0.01	5.86 (1.18 - 29.13)	0.03
Severe initial depression (0, 1 and 2)	3.93 (3.17 - 4.88)	<0.01	8.11 (4.92 - 13.35)	<0.01	2.34 (1.64 - 3.35)	<0.01	0.74 (0.11 - 5.06)	0.75
p for the trend	1.41 (1.34 - 1.48)	<0.01	1.39 (1.25 - 1.54)	<0.01	1.24 (1.14 -1.34)	<0.01	0.99 (0.69 - 1.43)	0.97

[each] column is a different IPW Cox model adjusted by the variables in Table 3: individual variables: maternal age, parity, prenatal controls, sex, gestational age, birth weight, type of delivery and comorbidities, and sociodemographic variables: type of health care (public or private), level of health care and numerical geographic area
Statistically significant values $P < 0.05$

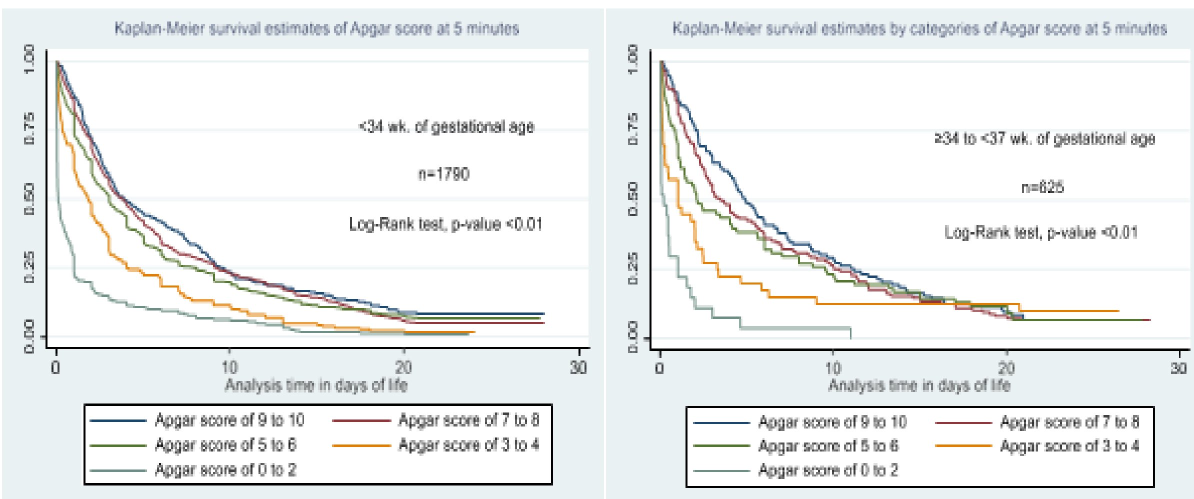

Figure 2. Kaplan Meier survival estimate according to Apgar score at 5 minutes, distributed according to gestational age with a follow-up cutoff at 21 days

Discussion

This study shows a strong and independent association between the Apgar score at 5 minutes and the risk of mortality in newborns. These results are consistent with other reports in which newborns at risk with a low Apgar score at 5 minutes were more likely to be admitted to the intensive care unit and had a higher probability of death than newborns with a high score [19;20].

According to the results found in a study, a low Apgar score (0-3) represents a 100 times greater risk of infant death; this is associated with anoxia or infection and hyaline membrane disease in newborns who are premature. This suggests that the Apgar score in neonates at risk has a high predictive capacity. Nevertheless, the risks associated with lower scores differ less than this scale's behavior and prognostic value in neonates who are not at risk.

Several investigations have determined that a low Apgar score in newborns is directly associated with neurodevelopmental problems and long-term mortality [13;21;22].

The association is independent of gestational age at birth and other prenatal, natal, postnatal, and sociodemographic determinants, in agreement with the preliterature [23;24].

There was no standardized categorization of the Apgar score at 5 minutes. However, the findings of this study suggest that a more disaggregated categorization would help to better estimate complications and death among newborns at risk.

It is essential to recognize that even if tools are used to predict unfavorable outcomes in newborns, there is still much room for action to be taken to reduce neonatal death in Latin America and the Caribbean [25;26;27]; it is necessary to expand the population's access to health services, ensure universal childbirth inadequate facilities, and guarantee the identification of possible scenarios that require emergency obstetric and neonatal interventions in a rapid and timely manner, especially in areas of difficult access or rural areas, reduce adolescent pregnancy rates, and improve antibiotic management of neonatal infections to mitigate bacterial resistance, among others [28;29].

In Ecuador, for example, the lack of effective interventions has affected neonatal mortality, causing it to increase from 4.6 to 6.0 neonatal deaths per 1,000 live births from 2014 to 2019 [30].

It can be said that a standardized Apgar score can help in decision-making during the early care of newborns at risk [11]; however, it should be added to the training of health personnel for neonatal care, the adequate supply of supplies, and a significant improvement in neonatal transport to substantially reduce the neonatal mortality rate in Ecuador.

On the other hand, even though a national database was used in this study, ensuring statistical power and minimizing confounding bias by including prenatal, natal, postnatal, and sociodemographic covariates, the main limitation was the evaluation of the quality of the Apgar score information used. In addition, the lack of information about the Apgar score at 1 minute and 10 minutes of life was another drawback, preventing a complete evaluation of this neonatal risk scoring system as a predictive tool.

It should be emphasized that even though the current Ecuadorian regulations include the use of the Apgar score as a mandatory process since it has been used for more than 25 years in the country (Lucio et al., 2011), from the design of research: systemic grounded theory carried out through a phenomenological analysis, it can be said that there is still a lack of specific knowledge about its application by health workers, being scarcely internalized in the different levels of care, both in the public and private sectors.

Conclusions

The APGAR assessment at 5 minutes predicts the survival of newborns; higher values are associated with more survival. The factors that increased the risk of mortality were adolescent and elderly maternal age, extreme premature gestational age, light weight, the presence of malformations, and neonatal asphyxia. The sociodemographic factors were births in first-level institutions and newborns born in zone 3 of Ecuador (Cotopaxi, Tungurahua, Chimborazo, and Pastaza).

Abbreviations

HR: hazard ratio.
Ptlb: per thousand live births
SPSS: Statistical Package for the Social Sciences.

Supplementary information

Supplementary materials are not declared.

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Author contributions

Andrea Elizabeth Aguilar Molina: Conceptualization, Data Retention, Funding, Research, Resources, Software, Writing - original draft.
Silvana Soledad Rivera Guerra: Conceptualization, Data Retention, Fundraising, Research, Resources, Software, Writing - original draft.
Ivan Guillermo Dueñas Espín: Conceptualization, Data Conservation, Supervision, Fundraising, Research, Resources, Writing: review and editing.
Daniel Maldonado: Data curation, research, fundraising, supervision, methodology.
All authors read and approved the final version of the manuscript.

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Availability of data and materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available through the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

It was not needed.

Publication consent

It does not apply to studies that do not publish MRI/CT/Rx images or physical examination photographs.

Conflicts of interest

The authors declare no conflicts of interest.

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