Perinatal outcomes in a hospital from southern Brazil: Predictors of low APGAR in the first minute of birth

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ABSTRACT

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Introduction: The Apgar Index (AI), is a method that assesses the physical conditions of the newborn (NB) in the period immediately after birth. The index proved to be a predictor of neonatal mortality in several clinical and population-based studies and has been used as a health assessment parameter in the immediate neonatal period for over 60 years.

Objective: To evaluate obstetric history and perinatal outcomes in newborns (NB) Apgar score equal zero in the first minute of life. Data from births in a public hospital in southern Brazil were evaluated. The studied population was divided into two groups: cases (AI equal zero) and controls (NB with AI ≥8). The cases were composed of 219 NB and the controls of 657 NB.

Results: In the multivariate analysis, the maternal variables predictors of AI zero in the first minute of life were: mother's age >25 years [odds ratio (OR): 1.8; confidence interval (95%CI): 1.1 – 2.8; p = 0.020] and absence of prenatal care (OR: 2.8; 95%CI: 1.5 – 5.5; p = 0.010). Death in the delivery room was higher in cases compared to controls (*p* < 0.001). Additionally, predictive neonatal variables were: umbilical arterial pH (<7.0) (OR: 5.2; 95%CI: 4.0 – 8.8; p <0.001), base excess (>-6.5) (OR: 4.1; 95%CI: 3.3 – 10.5; p <0.001), fetal breech presentation (OR: 7.1; 95%CI: 4.2 – 13.1; p <0.001), gestational age <33 weeks (OR: 15.1; 95%CI: 5.8 – 20.3; p <0.001), fetal weight <2500g (OR: 21.5; 95%CI: 12.1 – 31.9; p <0.001) and hemorrhagic amniotic fluid (OR: 13.8; 95%CI: 5.4 – 48.6; p <0.001).

Conclusion: Absence of prenatal care, maternal age, low birth weight, prematurity, breech presentation, hemorrhagic amniotic fluid, low AI in the fifth minute of life, lower umbilical artery pH values, and higher base excess values are related to AI zero in the first minute.

Keywords: Apgar score, Apgar zero first minute, perinatal outcomes.

INTRODUCTION

The Apgar Index (AI), created by Virginia Apgar in 1953, is a method that assesses the physical conditions of the newborn (NB) in the period immediately after birth[1,2]. The index proved to be a predictor of neonatal mortality in several clinical and population-based studies and has been used as a health assessment parameter in the immediate neonatal period for over 60 years[1,3]. Its action as a predictor of the need for resuscitation and reassessment led it to be incorporated into various protocols and in the health policy of the World Health Organization (WHO)[3]. The index ranges from 0 to 10 and is measured at the 1st and 5th minute postpartum, and can also be measured at the 10th minute[4,5]. It is known that an AI of zero (apparently dead fetuses) is indicative of mortality and, especially, severe neonatal morbidity[1]. The index assesses muscle tone, breathing, heart rate, reflex activity, irritability, and skin color, all to classify the degree of fetal asphyxia as absent (8-10), mild (5-7), moderate (3-4), or low (0-2)[6]. Each criterion receives an evaluation of 0-2 points, according to the evaluation of the professional who assists the NB[5-7].

In recent years, there are few studies related to the epidemiological analysis of neonates with AI zero in the 1st minute of life, as well as their associations with

obstetric and intrapartum history[1,8,9]. The frequency of births with AI zero ranged from 0.4 to 0.8/1,000 live births, and among these, mortality ranged from 28% to 57%. Survivors (14% to 60%) have neurological damage[9].

It is known that AI alone may not be related to fetal acidosis, especially in premature fetuses, as it is partially dependent on the maturity of the conceptus[10-13]. There are also few studies relating an AI of zero, or even less than five, with neonatal outcomes, as well as with maternal risk factors, labor, and mode of childbirth[1,9,14]. Other factors such as AI less than five in the 5th minute, time to subsequent resuscitation, time to reach a score equal to or greater than seven (time greater than ten minutes), and presence of seizure events in the first minutes of life are also associated with a worse prognosis. and a high neonatal mortality rate[1].

Despite the few and scarce studies in this area, it is known that NBs that are stillborn (AI zero in the 1st minute) are at greater risk for early death and adverse neurological outcomes, higher rates of resuscitation in the 1st minute, prematurity associated with low birth weight, fetal acidosis status, neurological impairments, and early mortality rate[3,6,9]. In addition, newborns who survive birth may develop neurological complications, namely epilepsy, cerebral palsy, and developmental delay[3,9]. The risk factors for perinatal asphyxia can be divided into antepartum, intrapartum, and fetal asphyxia, namely: pregnancy at the reproductive extremes of life, prolonged membrane rupture time, meconium amniotic fluid, absence of prenatal care, low birth weight, Antepartum hemorrhage, and anomalous presentations are risk factors related to low AI, consequent neonatal anoxia and need for treatment in a neonatal intensive care setting[3].

Given the importance of the topic and the scarcity of studies related to obstetric and perinatal history in cases of zero AI in the first minute, this case/control study was proposed at the Department of Gynecology and Obstetrics/Neonatology of a public hospital in southern Brazil.

METHODS

Study design and ethical issues

This is a case/control study nested within a cross-sectional study that analyzed, from May 1998 to December 2015, data from newborns from the Gynecology/Obstetrics and Neonatology Service of a public hospital in southern Brazil. The present study was approved by the Research Ethics Committee (protocol: 1.453.509).

Population studied

The population studied was divided into two groups:
Two groups were composed: Cases with 219 NB with AI equal zero in the first minute and controls with 657 NB (1:3 proportion about the number of cases) with AI ≥ 8.

Cases: where all births registered in the aforementioned period and which obtained AI equal zero in the first minute of life were included.

Controls: where the three NB with AI equal to or ≥8 in the first minute of life were randomly included in the same database, in a proportion of 3:1.

Inclusion criteria

All single pregnancies, with gestational age (GA) equal to or greater than 22 weeks or weight equal to or ≥500g, whose birth took place at a public hospital in southern Brazil were considered.

Exclusion criteria

Twin pregnancies, NB with GA less than 22 weeks or weight <500g, carriers of congenital anomalies, NB born outside the GH, and all medical records are incomplete or with inconsistent data.

Outcomes

Maternal: age (average); schooling (≥8 and <8 years); skin color (white and non-white); parity (primigravid and ≥2); weight at the beginning of pregnancy; tobacco and alcohol users; provision of prenatal care, mode of childbirth (vaginal and cesarean); type of amniotic fluid (meconium, hemorrhagic, or clear); hypertensive syndrome (composed of chronic hypertension, gestational hypertension, preeclampsia, preeclampsia superimposed on chronic hypertension, HELLP syndrome, and eclampsia) and diabetic syndrome (types 1 and 2 diabetes mellitus and gestational diabetes mellitus).

Neonatal: gestational age (mean, based on the date of last menstrual period and confirmed by early ultrasound or Capurro's method); fetal presentation (pelvic or cephalic); birth weight (500g up to 2500g and over 2,500g); umbilical artery pH and base excess; the need for treatment in a neonatal intensive care environment; AI in the fifth minute (median); early neonatal mortality (≥7 days); conditions of the newborns at the time of hospital discharge (death or discharge alive).

Statistical analysis

Data were analyzed using IBM SPSS® software, version 25.0 (Chicago, IL Statistical Package for the Social Sciences). For continuous data, normality was assessed using the Kolmogorov-Smirnov test, with Lilliefors correction. Student's t-test for independence samples was used to assess possible differences between the mean values in the study groups. Bivariate analyses were performed to assess the association between categorical variables, using Fisher's exact test or the chi-square test (as appropriate). The odds ratio (OR), as well as the respective 95% confidence interval

(95%CI), absolute and relative frequencies, were estimated for the categorical data using Pearson's chi-square test or Fisher's exact test. Multivariate analysis was performed by logistic regression. *P*-values <0.05 were considered statistically significant.

RESULTS

Table 1 presents the maternal variables analyzed in the study and is representative of the sample. The mean maternal age in cases was 26.8 ± 7.5 years and in controls, 25.3 ± 6.9 (*p* = 0.005). In the case group, the percentage of patients who had hypertensive syndrome was slightly higher than in the control group, with [14% (n=31) vs. 12% (n=81)], but without statistical significance. Regarding diabetic syndrome, the percentage of cases was lower than in controls [3% (n=7) vs. 7.5%(n=49); *p* = 0.038]. Most patients in both groups reported adequate prenatal care, although the percentage of patients without assistance was higher in cases [9.5% (n=20) vs. 3.4% (n=22); *p* <0.001]. The other variables did not show statistical significance.

Table 1: Distribution of maternal variables related to NBs with AI zero in the first minute in a case/control study of the Gynecology/Obstetrics and Neonatology Service of a public hospital in southern Brazil.

Variables	Cases (n=219)	Controls (n=657)	OR	CI95%	*p-values*
	n (%)	n (%)			
Age (mean ± SD)	26.8 ± 7.5	25.3 ± 6.9	-	-	**0.005**
Maternal weight (mean ± SD)	65.7 ± 15.6	66.2 ± 15.8	-	-	0.790
Years of schooling					
<8	49 (24.0)	210 (44.0)	0.39	0.27-0.57	**<0.001**
>8	158 (76.0)	267 (56.0)	1.0 (ref.)		
Self-declared skin color					
Not white	48 (24.5)	168 (26.0)	0.93	0.64-1.35	0.719
White	148 (75.5)	484 (74.0)	1.0 (ref.)		
Hypertensive syndrome					
Yes	31 (14.0)	81 (12.0)	1.17	0.75-1.81	0.559
No	188 (86.0)	576 (88.0)	1.0 (ref.)		
Diabetic syndrome					
Yes	7 (3.0)	49 (7.5)	0.41	0.18-0.91	**0.038**
No	212 (97.0)	608 (92.5)	1.0 (ref.)		
Prenatal					
No	20 (9.5)	22 (3.4)	3.2	1.62-5.67	**<0.001**
Yes	190 (90.5)	633 (96.6)	1.0 (ref.)		
Parity					
1	139 (64.0)	450 (68.5)	1.05	0.77-1.44	0.735
>2	79 (36.0)	207 (31.5)	1.0 (ref.)		
Smoking					
Yes	13 (24.0)	47 (17.0)	1.53	0.76-3.08	0.308
No	42 (76.0)	236 (83.0)	1.0 (ref.)		
Alcohol consumption					
Yes	3 (5.5)	4 (1.4)	3.98	0.86-18.31	0.090
No	52 (94.5)	276 (98.6)	1.0 (ref.)		

SD: Standard deviation; Ref.: reference category; Hypertensive syndrome (composed of chronic hypertension, gestational hypertension, preeclampsia, preeclampsia superimposed on chronic hypertension, HELLP syndrome, and eclampsia) and diabetic syndrome (types 1 and 2 diabetes mellitus and gestational diabetes mellitus); In bold, significant *p*-values are highlighted.

Table 2 presents the neonatal variables. In a comparison between cases and controls it was observed that: gestational age (in weeks) stands out (31.7 ± 5.8 vs. 38.7 ± 2.5; *p* <0.001), lower fetal weight at birth [(n=132 (75%) vs. n =12 (77); *p* <0.001], lower rates of umbilical artery pH (6.99 ± 0.22 vs. 7.25 ± 0.77; *p* <0.001), higher rates of base excess (-16.70 vs. -6.30; *p* <0.001), breech presentation [24% (n=44) vs. 4% (n=25); *p* <0.001] and a higher incidence of bleeding amniotic fluid during amniotomy [n=18 (9.1%) vs. n=4 (0.6%); *p* <0.001]. The mode of childbirth was similar in

both groups, with a majority of abdominal c-section delivery in both groups, although without statistical significance. The frequency of patients admitted to the ICU, the nursery evolution of early neonatal death, and death in the delivery room were higher in cases compared to controls ($p < 0.001$). In addition, the APGAR score at 5 minutes was significantly lower in cases compared to controls ($p < 0.001$).

Table 2: Distribution of variables related to newborns with Apgar zero in the first minute of life in a case/control study carried out at the Gynecology/Obstetrics and Neonatology Service of a public hospital in southern Brazil.

Variables	Cases (n=219) n (%)	Controls (n=657) n (%)	OR	CI95%	p-values
Umbilical arterial pH (mean ± SD)	6.99 ± 0.22	7.25 ± 0.77	-	-	**<0.001**
Base excess (mmol/L) (mean ± SD)	-16.7 ± 7.6	-6.3 ± 3.3	-	-	**<0.001**
Type of childbirth					
Cesarean	146 (72.0)	440 (77.0)	0.9	0.5-1.1	0.186
Normal	56 (28.0)	132 (23.0)	1.0 (ref.)		
Fetal presentation					
Pelvic	44 (24.0)	25 (4.0)	7.9	4.6-13.4	**<0.001**
Cephalic	140 (76.0)	600 (96.0)	1.0 (ref.)		
Gestacional age (mean ± SD)	31.7 ± 5.8	38.7 ± 2.5			**<0.001**
Fetal weight (g)					
500-2.499	132 (75.0)	77 (12.0)	22.6	14.9-34.2	**<0.001**
≥2.500	44 (25.0)	579 (88.0)	1.0 (ref.)		
Sex					
Male	23 (51.0)	149 (53.0)	0.9	0.5-1.8	0.956
Female	22 (49.0)	133 (47.0)	1.0 (ref.)		
Amniotic fluid					
Hemorrhagic	18 (9.1)	4 (0.6)	15.6	5.2-46.6	**<0.001**
Meconial	10 (5.1)	42 (6.7)	0.8	0.4-1.7	0.590
Translucent	169 (86)	584 (93)	1.0 (ref.)		

SD: Standard deviation; Ref.: reference category; In bold, significant *p*-values are highlighted.

In the multivariate analysis, the maternal variables predictors of AI <8 in the first minute of life were: mother's age >25 years (OR: 1.8; 95%CI: 1.1 – 2.8; $p = 0.020$) and absence of prenatal care (OR: 2.8; 95%CI: 1.5 – 5.5; $p = 0.010$). Additionally, predictive neonatal variables were: umbilical arterial pH (<7.0) (OR: 5.2; 95%CI: 4.0 – 8.8; $p < 0.001$), base excess (>-6.5) (OR: 4.1; 95%CI: 3.3 – 10.5; $p < 0.001$), fetal breech presentation (OR: 7.1; 95%CI: 4.2 – 13.1; $p < 0.001$), gestational age <33 weeks (OR: 15.1; 95%CI: 5.8 – 20.3; $p < 0.001$), fetal weight <2500g (OR: 21.5; 95%CI: 12.1 – 31.9; $p < 0.001$) and hemorrhagic amniotic fluid (OR: 13.8; 95%CI: 5.4 – 48.6; $p < 0.001$) (Table 3).

Table 3: Multivariate analysis to identify predictors associated with an AI outcome equal to zero in the first minute of life.

Variables	OR	CI95%	p-values
Mother variables			
Mother age (>25 years)	1.8	1.1 - 2.8	**0.020**
Maternal weight (<65 Kg)	1.1	0.5 - 1.9	0.297
Schooling (≤8 years)	1.9	0.4 - 2.7	0.157
Self-declared skin color (not white)	1.8	0.7 - 2.2	0.214
Hypertensive syndrome	1.2	0.8 - 5.5	0.312
Diabetic syndrome	0.5	0.7 - 5.3	0.302
Absence of prenatal	2.8	1.5 - 5.5	**0.010**
Parity (1)	1.1	0.7 - 1.88	0.267
Smoking	1.4	0.6 - 4.6	0.315
Alcohol consumption	2.5	0.4 - 5.1	0.247

Table 3: Continuation.

Variables	OR	CI95%	*p-values*
Neonatal variables			
Umbilical arterial pH (≤7.0)	5.2	4.0 - 8.8	**<0.001**
Base excess (mmol/L) (>-6.5)	4.1	3.3 - 10.5	**<0.001**
Type of childbirth (cesarean)	0.8	0.3 - 1.2	0.191
Fetal presentation (pelvic)	7.1	4.2 - 13.1	**<0.001**
Gestacional age (<33 weeks)	15.1	5.8 - 20.3	**<0.001**
Fetal weight (<2.500g)	21.5	12.1 - 31.9	**<0.001**
Male sex	0.7	0.4 - 1.9	0.914
Amniotic fluid (Hemorrhagic)	13.8	5.4 - 48.6	**<0.001**

In bold, significant *p*-values are highlighted.

DISCUSSION

In the present study, neonatal mortality in the delivery room of NBs with zero AI in the first minute was 4.6% (n=10), and early neonatal mortality (<7 days) was 88% (n=193). It is known that early neonatal mortality, especially in the first six days of life, is associated with obstetric, maternal, childbirth, and prenatal care factors[15]. The AI in the fifth minute was also low, ranging from 0 to 5, which characterizes the significant fetal acidemia and difficulty in recovering these NBs[3,5,8]. The group of cases also had lower umbilical artery pH values and higher rates of base excess when blood gas was obtained from the umbilical artery. To better identify situations that compromise fetal health, umbilical artery pH has been widely adopted as a complement to AI[1,16-19]. Fetal acidemia has been suggested as having pH <7.0. It is known, however, that labor can induce a transient acidemia with a pH that can drop to 7.0 without harm to the fetus[8,19], and that some NBs with low AI may have normal pH values[17,19]. Pathological fetal acidemia can be defined by an umbilical artery pH of <7.0, which characterized the cases NBs in this study and signaled an increased risk of neurological damage and multiple organ dysfunctions[16,18,19]. The identified condition of acidosis explains the high rate of need for NB treatment in a neonatal intensive care environment. Previous studies cite that cases of low AI at birth, associated with markers of fetal acidemia are related to higher rates of neonatal morbidity and mortality[8,10,16,19].

The profile of pregnant women included in cases and controls was characterized by a mean maternal age of 26.8 ± 7.5 vs. 25.3 ± 6.9, mostly white, the average weight of 65.7 ± 15.6 vs. 66.2 ± 15.8 and identical parity, data without statistical significance to configure the homogeneous distribution of the studied sample. Haddad et al.(2001)[9] analyzed the obstetric history of conceptuses dead with successful resuscitation and associated them with black and multiparous patients, as well as the mean age and weight similar to those of the present study. It is important to emphasize that maternal and neonatal complications in low-risk pregnancies are likely to occur unexpectedly in primiparous patients (41.0%), with at least one complication, then in multiparous patients (19%) with at least one complication[19]. Primiparous women tend to have more complications during childbirth since labor/childbirth is generally longer and has a higher rate of dystocia than multiparous women[7].

Kassar et al. (2013)[14] when studying the determinants related to neonatal death with a focus on prenatal care and birth identified that schooling, maternal age, and family income were also not independent risk factors for early neonatal death[20]. Regarding the use of alcohol and tobacco, although the patients in cases had a higher percentage of users compared to controls, this percentage was small and the results were not statistically significant. The difficulty in knowing the real rate of these dependencies is well known.

The gender of the newborns was also not related to the outcome studied in this study. As for the obstetric and prenatal variables, it was evidenced that patients who did not undergo prenatal care are three times more likely to have birthed with zero AI in the 1st minute. Adequate prenatal care has been presented as one of the main protective factors against low birth weight, prematurity, intrauterine growth retardation, and, mainly, neonatal deaths[1,9,20]. In the study, birth weight was subdivided into those born weighing <2,500g and ≥2,500g, since high-risk newborns tend to weigh <2,500g[6,20]. In this study, 75% of the patients with AI zero weighed <2,500g (OR = 22.6; *p* <0.001). In the study by Haddad et al. (2001)[9] fetal weight was also lower in the group of apparently dead fetuses (*p* <0.001), as well as in the study by Madi et al. (2011)[1] that showed that lower gestational age was associated with a higher chance

of zero AI (*p* <0.001), as in the previously mentioned studies[1,9]. It is known, however, that AI may not be adequately evaluated in premature fetuses[2,11].

Regarding the mode of childbirth, in previous studies, c-section delivery was presented as a risk factor for complications and early neonatal outcomes[1,9,18]. In the study carried out at a public hospital in southern Brazil, the mode of childbirth was not statistically significant. In the case group, the percentage of pregnant women who developed hypertensive syndrome (n=31; 14%) was slightly higher than in controls (n=81; 12%).

The present study has some limitations: i) It is an observational study, and the findings must be taken into account with caution, given the degree of evidence of this type of design; ii) Sampling was by non-probabilistic convenience, which may have possibly included some sample collection bias, even although all epidemiological care was taken in this process; iii) It was not possible to access some clinical information such as length of stay, case-mix, medications used during hospitalization and outcomes such as seizures.

CONCLUSION

The AI zero was associated with the absence or inadequacy of prenatal care, breech fetal presentation, hemorrhagic amniotic fluid, prematurity, fetal weight <2,500g, and low AI up to the fifth minute of life. In addition, newborns were 10 times more likely to have neonatal death in the delivery room and had a greater need for treatment in a neonatal intensive care environment, as evidenced by lower pH values and higher values of base excess. Among the maternal variables, age and absence of prenatal care were predictors of the AI <8 in the first minute of birth.

Authorship

Jonas Wolf designed and implemented the study. Jonas Wolf performed the statistical analyses. Jonas Wolf wrote the first draft of the manuscript and contributed to the literature review and discussion of the results.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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