Abstract
Neonatal depression leads to severe neurological sequelae with important impacts on quality of life. Most risk factors are sensitive to primary care actions, and this should be considered when developing prevention strategies. The aim was to identify the incidence and risk factors associated with neonatal depression in newborns at a Brazilian regional public hospital. A cross-sectional study of 784 live births with gestational ages of 22 weeks or more and without any major congenital anomalies was performed. Neonatal depression was defined as an Apgar score lower than seven at five minutes. Chi-square tests (p<0.05) were used for the analysis of associations, and a logistic regression model was run to control the confounding factors. The neonatal depression rate was 2.2%. Multivariate logistic regression revealed that the presence of foul-smelling amniotic fluid (OR=8.7, p=0.005) and the time of rupture of larger membranes (OR=37.5, p<0.001) were independently associated with neonatal depression. Risk conditions for perinatal infection and prematurity increase the likelihood of neonatal depression. Adequate prenatal care and guaranteed access to delivery services may reduce the occurrence of these neonatal depression risks and, consequently, may reduce infant morbidity and mortality.

Keywords: Asphyxia Neonatorum, Infant, Newborn, Risk Factors, Logistic Models, Primary Health Care.

Introduction
The main goal of neonatal care performed in the delivery room is to reduce infant morbidity and mortality, which promotes the survival of newborns (NBs) in the best possible functional conditions [1]. Neonatal depression is an injury that can lead to hypoxic-ischaemic syndrome, and it affects NBs irrespective of gestational age.

Each year, approximately 4 million NBs worldwide present asphyxia, with one million developing severe sequelae and one million who do not survive [2,3]. Neurological sequelae impart a lower quality of life and higher costs to maintain the individual within the family and society [4,5].

In 1953, anaesthesiologist Virginia Apgar proposed a method to rapidly and accurately evaluate the birth conditions of children in their first minutes of life. The Apgar score considers five clinical parameters and ranges from zero to sixteen [6]. Apgar values between seven and ten in the fifth minute are considered normal. Values less than seven are inversely associated with an increased risk of neonatal morbidity and mortality, even though they do not necessarily predict neurological sequelae or any unfavourable outcomes [7,8].

Prematurity, low birth weight and birth asphyxia have been identified as the main factors associated with health problems at birth around the world. Maternal and gestational characteristics, such as infections, multiple births, hypertensive disease, smoking, illicit drug use, strenuous labour, low maternal schooling, black race, and a previous history of preterm birth, have been associated with a higher risk of low Apgar score (below seven) [9].

These factors, in an isolated or an aggregated way, may lead to poor health outcomes for children, especially those in less favoured populations that depend on the public health system. However, such factors are potentially modifiable by the control and prevention actions that are performed in primary health care activities. This fact represents a possibility for reducing the incidence of neonatal depression and its consequences.
In light of this fact, knowing the gestational characteristics and birth conditions of children is fundamental to subsidizing effective interventions. The aim is to adopt clinical practices that have been adjusted for populations with greater risk to reduce the morbidity and mortality associated with this undesirable hypoxic-ischaemic insult [10].

Thus, the present study aims to identify the incidence and risk factors associated with neonatal depression in a Brazilian regional public hospital.

Methods

This cross-sectional study was carried out from April 1st to September 30th, 2013, in the maternity ward and neonatal intensive care unit (NICU) of a public hospital located in Santos, Brazil. This hospital belongs to the Brazilian Unified Health System (SUS)/State Department of Health and is considered a reference centre for high risk pregnancy, attending, free of charge, the population of Baixada Santista, which has an average of 1,500 births per year. The study sample consisted of all live births in this period, regardless of the type of delivery, with gestational ages greater than or equal to 22 weeks. The exclusion criterion was the presence of a major congenital anomaly, such as hydrocephalus, diaphragmatic hernia, or kidney agenesis.

Data collection was performed by using the information available in medical records from the care team. Neonatal depression was defined as an Apgar score below seven in the fifth minute of life [9,11,12]. We used neonatal depression as an indicator of neonatal asphyxia. Characteristics related to the mother, gestational period, delivery and the NBs’ first minutes of life were studied as risk factors. Among them, we studied premature amniorrhexis, meconium-stained amniotic fluid, preeclampsia, previous abortion, oligoamnion, intrauterine growth restriction (IUGR) and the presence of foul-smelling amniotic fluid (FSAF).

In addition, we investigated the rupture time of membranes, type of delivery and presentation of the foetus, use of anaesthesia, characteristics related to the mother, gestational period, delivery and the NBs’ first minutes of life [9,11,12]. We used neonatal depression as an indicator of neonatal asphyxia. Characteristics related to the mother, gestational period, delivery and the NBs’ first minutes of life were studied as risk factors. Among them, we studied premature amniorrhexis, meconium-stained amniotic fluid, preeclampsia, previous abortion, oligoamnion, intrauterine growth restriction (IUGR) and the presence of foul-smelling amniotic fluid (FSAF).

Results

Eight hundred and eleven births were recorded in the study period. Of these, 17 patients (2.1%) were not included because they were stillborn and ten (1.2%) were excluded because they had a major congenital anomaly at birth. Thus, 784 NBs composed the final sample.

The mean maternal age was 26 years, and 86% of mothers reported having a stable relationship with their partners. The majority (93.2%) of mothers reported some type of paid work; however, a third (28.1%) of mothers reported a study time equal to or less than eight years.

Adolescent pregnant women were under 20 years of age [13] and adequate prenatal care was a minimum of six visits performed during pregnancy [14]. NBs with a birth weight less than 2,500g were defined as low birth weight and gestational age less than 37 weeks was defined as prematurity.

The completed questionnaires were evaluated in terms of their internal consistency prior to data entry for analyses. Data were entered twice, and subsequent validation was conducted in order to correct errors. Stata statistical software package Version 14.0 (College Station, TX: StataCorp LP) was used to analyse the data.

Data consistency analysis and univariate descriptive statistics were performed for the continuous and categorical variables. A Pearson's chi-square test was used to compare categorical variables.

To adjust for confounding variables, a multivariate logistic regression analysis was performed using a "stepwise forward" technique in terms of odds ratio (OR) estimates. All variables with p≤0.20 were eligible for the final model and the results were statistically significant when p≤0.05.

This research received ethical approval from the Hospital Guilherme Álvaro – Santos ethics committee.

Table 1: Incidences of newborn birth characteristics and comparisons between the depressed non-depressed groups, Santos, Brazil, 2013

<table>
<thead>
<tr>
<th>Characteristics (categorical variables)</th>
<th>n</th>
<th>Depressed</th>
<th>Non-depressed</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight</td>
<td>782</td>
<td>76.5 (13/17)</td>
<td>12.5 (96/765)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>780</td>
<td>47.0 (8/17)</td>
<td>53.0 (405/763)</td>
<td>0.633</td>
</tr>
<tr>
<td>Prenatal care</td>
<td>727</td>
<td>53.3 (8/15)</td>
<td>83.7 (596/712)</td>
<td>0.005</td>
</tr>
<tr>
<td>Instrumental delivery*</td>
<td>783</td>
<td>35.3 (6/17)</td>
<td>53.7 (411/766)</td>
<td>0.133</td>
</tr>
<tr>
<td>Adolescent mother</td>
<td>782</td>
<td>17.6 (3/17)</td>
<td>18.6 (142/765)</td>
<td>0.924</td>
</tr>
<tr>
<td>Meconium fluid</td>
<td>747</td>
<td>14.3 (2/14)</td>
<td>15.1 (111/733)</td>
<td>0.995</td>
</tr>
<tr>
<td>PPV with supplemental O₂</td>
<td>774</td>
<td>93.7 (15/16)</td>
<td>6.4 (49/758)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OTI</td>
<td>774</td>
<td>73.3 (11/15)</td>
<td>1 (8/759)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac massage</td>
<td>774</td>
<td>13.3 (2/15)</td>
<td>0.13 (1/759)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*a caesarean or forceps; PPV: Positive pressure ventilation; OTI: Orotracheal intubation
*Chi-square test or Fisher’s exact test
between groups with and without neonatal depression.

Table 2 presents the incidences and OR with respective confidence intervals for the risk factors associated with depression at birth. The presence of foul-smelling amniotic fluid at birth (OR=48.9 - 95% CI 6.2-318.2), prematurity (OR=26.8 - 95% CI 8.0-114.4) and low birth weight (OR=22.6 - 95% CI: 7.2-71.0) presented the greatest risks for neonatal depression.

The final logistic regression model (Table 3) shows the unadjusted and adjusted ORs for various risk factors of neonatal depression.

**Discussion**

The aim of this research was to identify the incidence and risk factors associated with neonatal depression. The incidence of this condition in the studied population was 2.2%, and the risk factors that were independently associated with neonatal depression were prematurity, presence of foul-smelling amniotic fluid, and longer membrane rupture times.

In a nationally representative Brazilian sample, Souza (2003) [15] described a general incidence of neonatal depression of 2.2%, using the same definition as the present study used; however, there were regional variations. Thus, the incidence found in the present study corroborates the previously estimated rate in Brazil. The incidence in Brazil differs from worldwide neonatal depression rates, which range between three and six per 1000 live births. However, these rates have been estimated based on different diagnosis criteria, which makes comparisons between countries difficult [2].

The present study defined newborns with neonatal depression as those with Apgar scores below seven in the five-minute test. This cut-off has the potential to present good accuracy when it is applied in areas with limited available resources for a precise diagnosis [9,11]. This choice may have favoured sensitivity instead of specificity in the neonatal asphyxia diagnosis, which potentially resulted in an overestimation of the studied outcome.

Among the evaluated risk factors, we observed that eight newborns presented statistically significant associations with

**Table 2:** Incidences and odds ratios with respective confidence intervals (95% CI) of risk factors for depression at birth in Hospital Guilherme Alvaro, Santos, Brazil, 2013

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Yes</th>
<th>No</th>
<th>OR</th>
<th>(CI 95%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Birth weight*</td>
<td>Yes</td>
<td>No</td>
<td>22.6</td>
<td>7.2 – 71.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prematurity b</td>
<td>Yes</td>
<td>No</td>
<td>26.8</td>
<td>8.0 – 114.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time of rupture of larger membranes (hours)</td>
<td>&gt; 18</td>
<td>≤ 18</td>
<td>10.3</td>
<td>2.9 – 33.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of FSAF</td>
<td>Yes</td>
<td>No</td>
<td>48.9</td>
<td>6.2 – 318.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of prenatal visits</td>
<td>&lt; 6</td>
<td>≥ 6</td>
<td>0.2</td>
<td>0.1 – 0.6</td>
<td>0.001</td>
</tr>
<tr>
<td>General anaesthesia</td>
<td>Yes</td>
<td>No</td>
<td>14.3</td>
<td>1.5 – 138.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Premature amniorrhesis</td>
<td>Yes</td>
<td>No</td>
<td>4.5</td>
<td>1.2 – 16.7</td>
<td>0.012</td>
</tr>
<tr>
<td>IUGR</td>
<td>Yes</td>
<td>No</td>
<td>3.6</td>
<td>0.8 – 16.7</td>
<td>0.075</td>
</tr>
<tr>
<td>Instrumental delivery c</td>
<td>Yes</td>
<td>No</td>
<td>0.5</td>
<td>0.2 – 1.3</td>
<td>0.142</td>
</tr>
<tr>
<td>Oligoamnion</td>
<td>Yes</td>
<td>No</td>
<td>1.6</td>
<td>0.2 – 12.4</td>
<td>0.656</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Yes</td>
<td>No</td>
<td>0.7</td>
<td>0.1 – 5.1</td>
<td>0.695</td>
</tr>
<tr>
<td>Adolescent mother</td>
<td>Yes</td>
<td>No</td>
<td>0.9</td>
<td>0.3 – 3.3</td>
<td>0.924</td>
</tr>
<tr>
<td>Meconium fluid</td>
<td>Yes</td>
<td>No</td>
<td>0.9</td>
<td>0.2 – 4.2</td>
<td>0.929</td>
</tr>
</tbody>
</table>

*Birth weight less than 2.500g, *Gestational age less than 37 weeks, *caesarean or forceps

OR: Odds Ratio; CI: Confidence Interval; FSAF: Foul-Smelling Amniotic Fluid; IUGR: Intrauterine Growth Restriction

*Chi-square test
neonatal depression: prematurity, low birth weight, the presence of foul-smelling amniotic fluid, a time of membrane rupture greater than 18 hours, a lack of prenatal care, intrapartum general anaesthesia, the presence of premature amniorrhesis, and a maternal history of syphilis. However, prematurity, the presence of foul-smelling amniotic fluid and a longer rupture of ovarian membranes were the only risk factors that remained in the multivariate final model; thus, these factors were independently associated with neonatal depression.

One of the main risk factors described in the literature for neonatal depression is a gestational age less than 37 weeks. Sousa [18] (2003) and Campos [19] (2010) observed that the presence of neonatal depression was inversely proportional to the gestational age. Similar results were found in our study, where prematurity presented an independent and positive association with neonatal depression. Body immaturity and difficulty transitioning from the foetal circulation to the neonatal circulation are the main factors that contribute to this association.

Klein et al. [20] described that, during birth, an evaluation of vital signs with the Apgar score can be the first indicator of neonatal infection, with a correlation between a low five-minute test score and a higher risk of infection in the newborn. Longer times for membrane rupture and premature amniorrhesis predispose the mother and newborn to infectious diseases; these characteristics consequently lead to lower Apgar five-minute test scores. Chorioamnionitis, which has foul-smelling amniotic fluid as one of its clinical manifestations [21], also represents a risk for neonatal depression since it increases the risk of precocious neonatal sepsis. In our study, we observed that membrane rupture times greater than 18 hours and the presence of foul-smelling amniotic fluid showed independent and statistically significant associations with neonatal depression.

Lower birth weight is described by Sarinho et al. [22] as a determining factor of neonatal mortality. In Brazil, according to Guimarães and Melendez [23], the lower birth weight rate is 9.2%, with possible variations by region. In the present study, the lower weight birth rate was 13.9%, and it was significantly associated with neonatal depression; similar results were also found by Cunha et al. [12] in his research in a maternity ward in Rio de Janeiro in 2004.

In parallel, it was observed that most pregnant women had at least six prenatal consultations (82.9%), as has been observed in other reference hospitals [21]. This consultation rate can be explained by the fact that high risk pregnancies require higher care and result in higher adhesion to prenatal care regimens. In this study, having more prenatal consultations was shown as a protective variable for neonatal depression; this result corroborates what those described by Rosa et al. [24] in 1999. However, this association was not significant in the multivariate model, since prematurity and low birth weight are highly associated with a lack of or fewer prenatal consultations [25-27].

The present study identified prematurity, the presence of foul-smelling amniotic fluid and membrane rupture times greater than 18 hours as statistically significant risk factors that were independently associated with neonatal depression. This finding was further validated by including explanatory factors that have the potential to influence neonatal depression in the multivariate analysis; our approach provided a broad perspective, which is necessary for events that are triggered by multiple risk factors [26]. However, it is important to mention that the present study did not include other potential risk factors for birth depression, such as cardiotocogram abnormalities and maternal fever. Therefore, the internal validity of the results must be considered with caution.

In addition, it is noteworthy to mention that it is very important to prevent perinatal depression by systematically examining prenatal risk factors and giving interventions to newborns with risk factors, especially those with multiple risk factors, as the risk of presenting depression increases when more risk factors are present [27].

In this context, the results reinforce the need for direct adoption of preventive measures in prenatal care, with improvements in
primary health care for pregnant Brazilian women. The evidence from these findings indicates that, during the elaboration and execution of control and prevention strategies for neonatal depression, health policies should consider the effectiveness of prenatal consultations, which promote better care for pregnant women, especially those who have higher risks of premature birth and infectious diseases during pregnancy.

Acknowledgement

We would like to thank the participating mothers and the team of the Maternal Child Specialised Reference Hospital in Santos (Hospital Guilherme Álvaro), where the study was conducted.

References