JOURNAL OF PHARMACOLOGICAL CHEMISTRY AND BIOLOGICAL SCIENCES

Vol.: 1(1). pp.58-72, July-Aug
DOI: 10.36619/2674886x.2019.1.59.72
ISSN: 2674-886X

Prevalence and risk factors associated with perinatal asphyxia in newborn infants

Rejane Maria de Oliveira Holanda[1]; Ana Maria de Lima Dantas[1]; Ianara Mendonça da Costa[1]; Eudes Euler de Souza Lucena[1]; Lucídio Clebeson de Oliveira[1]; Luciana Cristina Borges Fernandes[1]; Eduardo Pereira de Azevedo[2]; Francisco Irochima Pinheiro[2]; Amália Cinthia Meneses do Rêgo[2]; Irami Araújo-Filho[2] and Fausto Pierdoná Guzen[1,2]*

[1]Laboratory of Experimental Neurology, Department of biomedical sciences, Health Science Center, State University of Rio Grande do Norte, Mossoró-RN, Brazil.

[2]Post-graduation, Program in Biotechnology, School of Health, Potiguar University, Natal-RN, Brazil.

*Corresponding author: Full Professor Dr. Fausto Pierdoná Guzen. Current Address: Laboratory of Experimental Neurology, Department of Biomedical Sciences, Health Science Center, State University of Rio Grande do Norte, Mossoró/RN, Brazil. E-mail address: **fauguzen@usp.br**

Keywords:

Perinatal asphyxia
Prevalence
APGAR scoring
Newborn

Abstract

Introduction: Perinatal asphyxia is defined as an injury to the fetus or to the newborn caused by lack of oxygen (hypoxia) and/or lack of perfusion to some organs (ischemia), which is enough to induce biochemical and functional consequences. **Objective**: To determine the prevalence and main risk factors associated with perinatal asphyxia in a group of neonates. **Methods**: This is a cross-sectional, quantitative and descriptive exploratory study, conducted through interviews with puerperal women

who gave birth in hospitals located in a city of the Rio Grande do Norte state, Brazil. 1079 individuals participated of the study where 18 cases of asphyxiated newborns were identified. The inclusion criteria were neonates born with at least 22 weeks of gestational age with Apgar score lower than 3 in the first minute or less than 7 in the fifth minute (study group) compared to the control group (Apgar equal to or greater than 8 and 10 in the first and fifth minutes, respectively). **Results**: Multivariate analysis revealed an association between perinatal asphyxia with the number of prenatal consultations (1.293-1.779, P = 0.030), uterine bleeding (0.021-0.934, P = 0.042) and sedation of the mother (0.009-0.203, P = 0.001). After logistic analysis, the variables that remained in the model were anemia (1.820-40.874, P = 0.031), high risk of preterm birth (2.323-31.529, P = 0.009), pregnancy bleeding (1.934-25.691, P = 0.015) and hospitalization during pregnancy (1.174-8.247, P = 0.016). **Conclusion**: Information about the birth profile can direct the actions of perinatal care and the conduction of preventive practices toward pregnant women with the purpose of reducing the likelihood of perinatal asphyxia.

Introduction

Perinatal asphyxia is defined as an injury to the fetus or to the newborn caused by lack of oxygen (hypoxia) and/or lack of perfusion to some organs (ischemia), which is enough to induce biochemical and functional consequences. In fact, perinatal asphyxia is a major cause of morbidity and mortality in developing countries as it stands out with an incidence of 100-250/1000 live births, compared with 5-10/1000 in developed countries (Lawn *et al*., 2009).

Overall, the main causes of neonatal death are infections (35%), premature births (28%) and perinatal asphyxia (23%) (Ariff *et al*., 2010), where the latter accounts for 3.5 million neonatal deaths annually, of which 98% occurs in low- and middle-income countries (Black *et al.*, 2010). Latest data on global health indicates that neonatal deaths declined from 4.4 million in 1990 to 3 million in

2011. However, the leading causes of neonatal mortality in 2015 were still due to prematurity complications such as perinatal asphyxia and sepsis (WHO, 2017). Around four million newborns present asphyxia per year in the world and of these, one million develop severe sequelae and about the same number end up dying (Majeed *et al.*, 2007, Cruz & Ceccon, 2010). There are several risk factors related to perinatal asphyxia including maternal age less than 16 or greater than 35 years old, gestational age below 39 or above 41 weeks, gestational hypertension, diabetes, use of illicit drugs and alcohol, maternal infection, decreased fetal activity, uterine bleeding around the second or third trimester, weight discrepancy, fetal malformation, lack of antenatal care, caesarean delivery and general anesthesia (Almeida, Ginsburg & Anchieta, 2016, Garfinkle *et al.*, 2017).

Despite the continuous advances in maternal and child health services, many infants continue to be born without life or with pathologies already known and often avoidable even with the expansion of resources and new technologies. This is the case of perinatal asphyxia, which despite having a relatively low prevalence, has been associated with high rates of morbidity and mortality (Oswyn & Vince, 2000).

Therefore, perinatal asphyxia consists of an important study topic due to its prevalence in the Units of Neonatal Intensive Care around the world. Moreover, the occurrence of perinatal asphyxia lead to consequences to the society and to the children that have been diagnosed with asphyxia as they often result in serious sequela such as cerebral paralysis. For the best of our knowledge, there is no documented report on the main risk factors that contribute to perinatal asphyxia, despite its influence on neonatal morbidity and mortality. In this perspective, since perinatal asphyxia and its consequences can be prevented, especially when the risk factors are early identified, the present study aims to investigate the prevalence and the risk factors associated with perinatal asphyxia using a group of neonates born in a hospital.

Methods

This research was a cross-sectional, quantitative and descriptive exploratory study that was carried out with puerperas who gave birth in two hospitals.

Sample size

In order to determine the sample size, a population of 1553 labors was considered, in addition to a prevalence of 0.5 and a standard error of 0.05. After applying the inclusion and exclusion criteria described below, a sample of 307 pregnant women was used in this study.

Inclusion and exclusion criteria

The inclusion criteria used in this study were live newborns with at least 22 weeks of gestational age, defined by the date of the last menstrual period and corrected by the ultrasound examination of the first trimester of pregnancy, and diagnosed with Apgar Index lower than 3 in the first minute or less than 7 in the fifth minute. The exclusion criteria were live newborns with gestational age less than 22 weeks, those classified according to WHO as abortion and those born with Apgar Index of zero, which avoided any conflict with fetal or perinatal death.

Data collection

The data was collected through a survey based on the questionnaire of the national health research - Brazil, designed by the Osvaldo Cruz Foundation (FIOCRUZ) (NHS, 2010), as well as on the questionnaire designed by the Brazilian Ministry of Health (Brasil, 2010), which is entitled “Assessment of prenatal care and children under one year of age from the North and Northeast regions of Brazil”. Maternal information was obtained from the individual prenatal record of each puerperal woman, as well as from their medical files. Information related to the newborn was also obtained from his/her medical file.

Ethical aspects

This study complies with the

guidelines of the National Health Council (NHC) of the Brazilian Ministry of Health (Resolution 466/12), with the commitment to offer maximum benefits and minimum risks to all subjects involved in the study.

This research was previously approved by the Ethics and Research Committee of the State University of Rio Grande do Norte, under the protocol number 23742613.9.0000.5294.

Data collection

At birth, the Apgar score was used as a benchmark for assessing newborn's conditions. The scores obtained in the first and fifth minutes were recorded in each newborn's chart.

The independent variables were maternal age (in years), marital status, occupation, gestational age, cephalic presentation (demonstrated by ultrasonography), type of delivery, delivery at the first target hospital, anesthesia, sedation, use of medication during pregnancy, hospitalization during pregnancy, anemia during pregnancy, uterine bleeding, threatened labor, weight gain during pregnancy, number of pregnancy contractions, previous vaginal or cesarean delivery, maternal prenatal care, number of pregnancy examinations, number of consultations during prenatal care, professional care during pregnancy and the time period when the prenatal care started.

Statistical analysis

The database was built in the statistical software SPSS 22.0 (Statistical Package for the Social Sciences). After the final structuring of the database, a descriptive analysis of the sociodemographic variables was performed. Associations between perinatal asphyxia and sociodemographic, obstetric and reproductive variables were verified by square ($\chi 2$) and Fisher's exact tests. In addition, the Odds Ratio (ORs) and their respective confidence intervals (95%) were used to verify the magnitude of these associations.

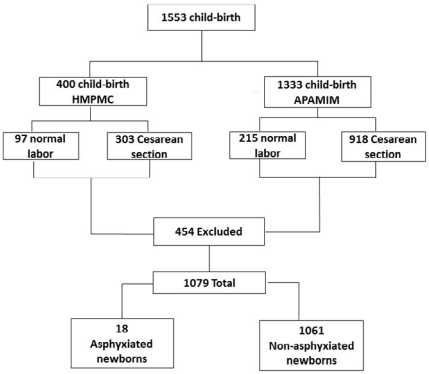
In order to know the predictive factors, the Logistic Regression was used through the hierarchical analysis (forward) to

estimate the ORs for perinatal asphyxia. The modeling was initiated by the most significant variables and then the other variables were added one by one, accepting a critical p value <0.05 for composing the model. The variable remained in the multiple analysis through the Likelihood Ratio Test, absence of multicollinearity, as well as its ability to improve the model through the Hosmer and Lemeshow test. Finally, the residues were analyzed to isolate the cases that exerted an undue influence on the model, causing little adherence. For all tests, a significance level of 5% was used.

Results

During the time period that this study was conducted, 1533 deliveries took place, where 400 births occurred, being 97 through vaginal delivery and 303 through cesarean. On the other hand, 1133 deliveries took place at Association of Maternity Care and Protection Hospital, of which 215 were vaginal deliveries and 918 cesareans. After applying the aforementioned exclusion criteria, 1079 women with their respective newborns were analyzed, where 18 neonates were classified as asphyxiated and 1061 as non-asphyxiated. The systematic of this study is represented in the flowchart outlined in Figure 1.

Figure 1: Flowchart depicting the process of screening and sample selection for this study.



By analyzing the age distribution of the mother, it was found that the range 24-34 years old was the one with the highest number of patients (503 or 47.9%) followed by the age group from 13 to 23 years old, with 454 patients (43.2%). The majority of the patients were single (38.8%) against 35.5% of married and most are housewives.

The Mulher Parteira Maria Correia Hospital is reference for high-risk pregnancy, receiving patients from neighboring cities, as well as patients who have been treated at this hospital and are classified as high-risk pregnants. In most cases, the patient has been previously admitted to a local hospital before being transferred to Mulher Parteira Maria Correia Hospital. They often arrive at this hospital handicapped and accompanied by professionals qualified for such care, until they reach the place where the delivery takes place. It was observed that women that were transferred from their local hospitals to the reference hospital (Mulher Parteira Maria Correia) were four times more likely to deliver an asphyxiated newborn.

The use of prescribed medication during pregnancy revealed that folic acid, ferrous sulfate and multivitamins were the most commonly used, although they were not associated with the incidence of perinatal asphyxia.

Regarding the characteristics of the amniotic fluid, 66.7% presented green amniotic fluid (LA). This information was collected from the patients and confirmed through their medical records (dark-stained meconium fluid). The meconium fluid is considered an indicator of "stress" (or fetal distress), especially in the presence of hypoxia or acidosis. Thus, meconium clearance has been used as a useful marker of intrauterine asphyxia. The newborns who presented Apgar index less than 7 in the 1st or 5th minute were headed to the newborn intensive care unit (93.8%). These newborns had up to eight times more chances to present asphyxia.

In this study, prolonged labor was a relevant factor for the occurrence of perinatal asphyxia. Longer labor increased more than fourfold the chance of perinatal asphyxia. Regarding the influence of intercurrences during pregnancy, hyperemesis gravidarum, uterine bleeding and urinary tract infection were found to be the major causes of intercurrence in the

gestational period. In addition, this study found that low birth weight (newborns weighing less than 2 kg) resulted in more than fivefold increase in perinatal asphyxia.

Regarding the level of schooling, the pregnant women who completed only high school were ten times more likely to present asphyxiated newborns than the puerperas who attended/completed some college.

The bivariate analysis shows that women with preterm gestational age, with first-time delivery, who were sedated, who had previous uterine contractions, who had uterine bleeding, anemia, threatened delivery, who were hospitalized during pregnancy and those who did not go through preterm care showed significantly higher chances of having babies with perinatal asphyxia (Table 1). After performing the final modeling of the logistic regression, only the variables sedation, prenatal follow-up and uterine bleeding remained significant (Table 2).

Table 1. Association of perinatal asphyxia with sociodemographic, obstetric and reproductive variables.

Variable	Asphyxia (positive)		Asphyxia (negative)					
Marital status (married)	n	%	n	%	x^2	OR	p value	IC
Yes	6	1.7	355	98.3	0.000	0.909	1.000	0.344-2.400
No	12	1.8	644	98.2				
Age	n	%	n	%	x^2	OR	p value	IC
13 to 23 years old	12	2.6	442	97.4	3.182	2.626	0.074	0.993-6.942
24 to 45 years old	6	1.0	590	99.0				
Gestational age	n	%	n	%	x^2	OR	p value	IC
Preterm	5	4.9	98	95.1	3.728	3.172	0.054	1.140-8.820
Fullterm/prolonged	12	1.5	772	98.5				
Performed cephalic ultrasonography	n	%	n	%	x^2	OR	p value	IC
Yes	14	1.5	948	98.5	3.314	0.302	0.069	0.102-0.897
No	4	4.8	79	95.2				
Type of delivery	n	%	n	%	x^2	OR	p value	IC
Vaginal	5	2.1	229	97.9	0.102	1.371	0.749	0.494-3.806
Cesarean	13	1.6	821	98.4				
Delivery at the first target hospital	n	%	n	%	x^2	OR	p value	IC
Yes	07	0.9	788	99.1	10.719	0.214	0.001	0.084-0.546
No	11	4.1	256	95.9				
Anesthesia	n	%	N	%	x^2	OR	p value	IC
Yes	12	1.5	783	98.5	0.001	0.679	1.000	0.090-5.109
No	1	2.2	44	97.8				
Sedation	n	%	n	%	x^2	OR	p value	IC
Yes	4	14.3	24	85.7	22.770	12.873	0.001	4.217-39.293
No	9	1.1	802	98.9				
Used prescription drugs during pregnancy	n	%	n	%	x^2	OR	p value	IC
Yes	15	1.5	1014	98.5	2.253	0.219	0.133	0.052-0.914
No	2	6.7	28	93.3				
Hospitalization during pregnancy	n	%	n	%	x^2	OR	p value	IC
Yes	10	2.9	331	97.1	4.574	3.050	0.032	1.171-7.944
No	7	1.0	721	99.0				
Anemia	n	%	n	%	x^2	OR	p value	IC
Yes	2	11.8	15	88.2	5.312	7.728	0.021	1.925-31.016
No	16	1.5	1035	98.5				
Uterine bleeding	n	%	n	%	x^2	OR	p value	IC
Yes	3	9.4	29	90.6	7.485	6.481	0.006	1.974-21.275
No	15	1.4	1022	98.6				
Threat of premature birth	n	%	n	%	x^2	OR	p value	IC
Yes	3	11.1	24	88.9	9.602	7.719	0.002	2.374-25.100
No	15	1.4	1027	98.6				
Weight increase	n	%	n	%	x^2	OR	p value	IC

Table 2. Final logistic regression model for the relation between perinatal asphyxia and the gestational variables.

Variables	B	S.E.	Wald	P valor	Exp (B)	IC
Delivery at the first target hospital	1.103	0.691	2.545	0.111	3.012	0.777-11.678
Sedation	-3.169	0.803	15.580	0.001	0.042	0.009-0.203
Threat of premature delivery	-0.978	1.152	0.720	0.396	0.376	0.039-3.599
Uterine bleeding	-1.966	0.968	4.124	0.042	0.140	0.021-0.934
Uterine contractions	-1.192	0.698	2.916	0.088	0.304	0.077-1.193
Prenatal care	2.719	1.256	4.686	0.030	15.170	1.293-1.779
Anemia	-2.408	1.279	3.545	0.060	0.090	0.007-1.104
Hospitalization	-0.364	0.771	0.223	0.637	0.695	0.153-3.148
Gestational age	-0.438	0.817	0.288	0.591	0.645	0.130-3.197

Discussion

Perinatal asphyxia is a serious clinical problem worldwide that has significantly contributed to newborn mortality and morbi-

dity (Pitsawong, 2011). It is the fifth largest cause of mortality among children under five years old (Ilah *et al.*, 2015). In addition, among the asphyxiated neonates who survive, the great majority develop long-term sequelae (Butt, Farooqui & Khan, 2008).

This study showed that the occurrence of asphyxia was significantly higher in neonates whose mother did not go through prenatal care during pregnancy, regardless of being submitted to sedation or having episodes of bleeding. Previous reports corroborate our findings that the non-attendance of the mother to prenatal care is a risk factor for perinatal asphyxia (Majeed *et al*., 2007, Kaye, 2003, Aslam *et al*., 2014). In order to reduce the high incidence of asphyxia, health education programs and information activities about the importance of strictly following the prenatal care are highly recommended for the early detection of high-risk pregnancies and therefore, to reduce the likelihood of perinatal asphyxia (Ilah *et al*., 2015).

We truly believe that the purposes of prenatal care activities, at the various levels of health care, need to be reformulated in order to reiterate the importance of proper health education towards not only to pregnancy, but also in relation to complications that may arise during childbirth, such as asphyxia, that bring serious consequences to the newborns (Ogunlesi, Fetuga & Adekanmbi, 2013). This current study also showed that the occurrence of uterine bleeding was a significant factor that contributed to perinatal asphyxia, where this finding is in accordance with other previously reported studies (Majeed *et al*., 2007, Lee *et al*., 2008, Tabassum, Rizvi & Ariff, 2014).

In addition, the results of this study indicate that the use of anesthetics and sedatives can significantly increase the chances of perinatal asphyxia and therefore, are considered as important risk factors. In fact, other studies have shown that sedative/anesthetics drugs may diffuse through placenta and have indirect effects on the fetus (Sessler & Wilhelm, 2008). Such drugs may affect the blood pressure of the pregnant woman and therefore, her ability to trans-

port oxygen through placenta. Since oxygen transfer depends on the partial oxygenation pressure gradient between the maternal blood in the intervillous space and fetal blood in the umbilical arteries, the reduction in the mother's blood pressure can possibly impart the oxygenation of the fetus (Velde & Buck, 2012, Griffiths & Campbell, 2015).

In order to have a normal fetal oxygenation it is essential to maintain a proper uteroplacental perfusion. Thus, intrauterine asphyxia has been associated with the use of anesthesia for maternal surgery (Habib, 2012). In fact, prolonged maternal hypoxemia leads to fetal hypoxia, which can result in fetal death. Thus, any drug that causes deep maternal hypoxemia is considered a potential threat to the fetus.

Several studies have also found a significant association between intrapartum sedation and perinatal asphyxia (Pitsawong, 2011, Lee *et al.*, 2008, Wongsang, 2000, Milsom *et al*., 2002). They observed that the opioid drugs morphine and pethidine easily cross the placenta, where they have a half-life of around 13 hours in the newborn's system (Acog, 2002). In addition, pain-relieving narcotics used during childbirth can cause respiratory depression in the newborn. However, it is worth to point out that such drugs are of optional use, whose proper selection and adequate attention to the time of administration are fundamental and might reduce the likelihood of problems towards the mother and the newborn (Pitsawong, 2011).

In our study maternal anemia was also considered a significant risk factor for perinatal asphyxia, which is similarly reported by Nauman Kiyani, Khushdil & Ehsan (2014) and Majeed *et al.*, (2007), where 58% and 60% of the mothers had anemia at the time of delivery, respectively. In this regard, it seems reasonable to hypothesize that maternal anemia occurs due to hypoxia during labor (Nauman Kiyani, Khushdil & Ehsan (2014).

Previous studies have also indicated that preterm birth is one of the main risk factors associated with perinatal asphyxia (Yadav & Damke, 2017, Pitsawong, 2011,

Ilah *et al.*, 2015) probably due to the immaturity of the newborn preterm infants' pulmonary system, leading to respiratory failure (Lee *et al*., 2008).

Concerning uterine contractions, this study showed that the presence of contractions of high intensity and frequency was a factor that contributed to perinatal asphyxia. This finding also corroborates with previous reports, where the authors attribute the occurrence of perinatal asphyxia to the temporary interruption of placental blood supply, which occurs when the intramyometrial pressure exceeds maternal mean arterial pressure due to the multiple uterine contractions. Prolonged asphyxia can result in newborns with severe respiratory distress, with permanent central nervous system disorders and ultimately death (Salvo *et al*., 2007).

Another risk factor that presented high correlation with asphyxia was predelivery hospitalization, which is in accordance with the findings reported by Kaye[16], whose study was conducted in a hospital located in Kampala, East Africa. According to his study, the most relevant factors that contributed to perinatal asphyxia were predelivery hospitalization, prepartum or intrapartum anemia and hemorrhage (Kaye, 2003).

Our current study found a significant correlation between the threat of preterm birth with perinatal asphyxia. Threat of preterm birth is related to premature rupture of the membrane and to the premature displacement of the placenta. Premature rupture of the membranes is defined as a condition in which the rupture of the amnion/chorion membrane occurs more than one hour before the onset of labor (Aslam *et al*., 2014).

In accordance with previous studies (Majeed *et al*., 2007, Kaye, 2003), there is a relationship between the threat of preterm birth and clinical complications due to neonatal asphyxia as well as between preterm labor with rupture of the membranes.

Conclusion

Information about the birth profile can direct the actions of perinatal care and the conduction of preventive practices toward

pregnant women with the purpose of reducing the likelihood of perinatal asphyxia.

References

Almeida MFB, Ginsburg R, Anchieta LM. Neonatal resuscitation: Guidelines for health professionals. Brazilian Society of Pediatrics 2016.

American College of Obstetricians and Gynecologists: Obstetric analgesia and anesthesia. Int J Gynecol Obstet 2002. 78:321-35.

Ariff S, Soofi SB, Sadiq K, Asher BF, Shuaib K, Sadiqua NJ et al. Evaluation of health workforce competence in maternal and neonatal issues in public health sector of Pakistan: an assessment of their training needs. BMC Health Serv Res 2010; 10:319.

Aslam HM, Saleem S, Afzal R, Iqbal U, Saleem SM, Shaikh MWA, et al. "Risk factors of birth asphyxia." Ital J Pediatr [Internet]. 2014 Dec 20;40:94. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4300075/

Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet 2010; 375:1969-87.

Butt TK, Farooqui R, Khan MAU. Risk factors for hypoxic ischemic encephalopathy in children. J Coll Physicians Surg Pak. 2008 Jul;18(7):428–32.

Cruz ACS, Ceccon MEJ. Prevalence of perinatal asphyxia and hypoxic-ischemic encephalopathy in term newborns considering two diagnostic criteria. Rev Bras Cresc Desenvolv Hum 2010; 20:302-316.

Garfinkle J, Wintermark P, Shevell MI, Oskoui M. Children born at 32 to 35 weeks with birth asphyxia and later cerebral palsy are different from those born after 35 weeks. J Perinatol. 2017.

Griffiths SK; Campbell JP. Placental structure, function and drug transfer. Contin Educ Anaesth Crit Care Pain 2015. 15: 84-89.

Habib AS. A review of the impact of phenylephrine administration on material hemodynamics and material and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. Anesth Analg 2012; 114: 377-390.

Ilah BG, Aminu MS, Musa A, Adelakun MB, Adeniji AO, Kolawole T. Prevalence and Risk Factors for Perinatal Asphyxia as Seen at a Specialist Hospital in Gusau,

Nigeria. Sub-Saharan African J Med. 2015;2(2):64.

Kaye D. Antenatal and intrapartum risk factors for birth asphyxia among emergency obstetric referrals in Mulago Hospital, Kampala, Uganda. East Afr Med J. 2003 Mar;80 (3):140–3.

Kerdarunsree A. Prevalence and factors associated with birth asphyxia in Ratchapiphat Hospital. Vajira Med J 2004. 48: 79-86.

Lawn JE, Lee ACC, Kinney M, Sibley L, Carlo WA, Paul VK et al. Two million intrapartum-related stillbirths and neonatal deaths: Where, why, and what ca be done? Int J Gynecol Obst 2009; 107:5-18.

Lee ACC, Mullany LC, Tielsch JM, Katz J, Khatry SK, LeClerq SC, et al. Risk factors for neonatal mortality due to birth asphyxia in southern Nepal: a prospective, community-based cohort study. Pediatrics. 2008 May;121(5):e1381-90.

Majeed R, Memon Y, Majeed F, Shaikh NP, Rajar UDM. Risk factors of birth asphyxia. J Ayub Med Coll Abbottabad 2007. 19 (3):67–71.

Milsom I, Ladfors L, Thiringer K, Niklasson A, Odeback A, back A et al. Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. Acta Obstet Gynecol Scand 2002. 8: 909–17.

Ministério da Saúde. Avaliação da atenção ao pré-natal, ao parto e aos menores de um ano na Amazônia Legal e no Nordeste, Brasil, 2010. Ministério da Saúde. 2013. 1: 120-123.

National Health Survey (NHS) [Homepage on the Internet]. Rio de Janeiro: Oswaldo Cruz Foundation [Updated 2010; cited 2017 April 25]. Module N - Prenatal Care.

Nauman Kiyani A, Khushdil A, Ehsan A. Perinatal Factors Leading to Birth Asphyxia among Term Newborns in a Tertiary Care Hospital. Iran J Pediatr [Internet]. 2014

Oct 12; 24(5):637–42. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4359420/

Ogunlesi TA, Fetuga MB, Adekanmbi AF. Mothers' knowledge about birth asphyxia: the need to do more! Niger J Clin Pract. 2013;16(1):31–6.

Oswyn G, Vince JD.; Friesen H. Perinatal asphyxia at Port Moresby General Hospital: a study of incidence, risk factors and outcome. P N G Med J 2000. 43:110-20.

Pitsawong C. Risk Factors Associated with Birth Asphyxia in Phramongkutklao Hospital. 2011;19 (4):165–71.

Salvo HF, Flores JÁ, Alarcón JR, Nachar RH, Paredes AV. Factores de riesgo de test de Apgar bajo em recién nacidos. Rev. Chil. Pediatr 2007. 78: 253-260.

Sessler C, Wilhelm W. Analgesia and sedation in the intensive care unit: an overview of the issues. Crit Care 2008.12: 1-4.

Tabassum F, Rizvi A, Ariff S. Risk Factors Associated with Birth Asphyxia in Rural District Matiari, Pakistan: A Case Control Study. Int J Clin Med [Internet]. 2014; (December):1430–41.

Velde MV, Buck F. Fetal and Maternal Analgesia/Anesthesia for Fetal Procedures. Fetal diag. and Therapy 2012. 31: 201-209.

Wongsang N Risck factors associated with birth asphyxia in Samutprakarn Hospital. Bull Dept Med Serv 2000. 25: 78-86.

World Health Organization .Monitoring health for the SFGS sustainable development goals. Geneva: WHO Press, World Health Organization; 2016. Available at: http://www.who.int/gho/publications/world_health_statistics/2016/en/. Acessed Abril 23, 2017.

Yadav N, Damke S. Study of risk factors in children with birth asphyxia. 2017; 4 (2):518–26.