Univariate Analysis of Prenatal Risk Factors for Low Umbilical Cord Artery pH at Birth

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Abstract. Objective: To identify potential risk factors for low umbilical cord artery pH in term, singleton pregnancies. Methods: Retrospective case-control study. Cases were deliveries characterized by umbilical cord artery $pH \leq 7.05$. Controls were with no sign of hypoxia. Results: In the database of 10637 deliveries, collected between 2014 and 2015 at the University Hospital in Brno delivery ward, we identified 99 cases. Univariate analysis of clinical features was performed. The following risk-factors were associated with low pH: the length of the first stage (odds ratio (OR) 1.40 (95 % CI 1.04–1.89)) and the length of the second stage of labor (OR 2.86 (95 % CI 1.70–4.81)), primipara (OR 2.99 (1.90–4.71)) and meconium stained fluid (OR 1.60 (1.07–2.38)). Conclusion: Among the risk factors that increase the chance of low umbilical cord artery pH at term, we identified: excessive length of the first and second stage of labour, parity, and meconium stained fluid.

1 Introduction

The main focus of intrapartum cardiotocography (CTG) evaluation is on revealing possible occurrences of fetal hypoxia during delivery. Since CTG traces are not evaluated in a vacuum, it is of great importance to be aware of clinical features related to low pH outcomes in the newborn cord artery blood. Although many clinical factors have been documented in the literature as increasing the risk for mother and child during delivery, no study has attempted to connect clinical features with the objective outcome in form of umbilical cord artery pH.

In previous works, the main interest focused on risk factors related to Caesarean section. Gareen et al. [7] investigated the relation between maternal age and rate of Caesarean section. Patel et al. [13] published a study on a population of over 12 000 deliveries describing in great detail the relation between various risk factors and Caesarean section. Verhoeven et al. [18] investigated factors leading to Caesarean section in multiparous women.

Other studies have also investigated risk factors influencing birth outcomes, e.g. the study by Martius et al. [12] focusing on pre-term delivery risk factors

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for various degrees of prematurity, and on an assessment of factors contributing to a prolonged labor, e.g. Szal [16].

When searching for relevant research papers, we used the phrase "risk factors for birth asphyxia". This yielded 20 results, out of which only four seemed relevant to the study at hand [1,3,8,9]. We should note here that in both cases the asphyxia was related to the Apgar score – which is a subjective measure and is considered to be only a crude descriptor of asphyxia [10]. A retrospective study by Aslam et al. [1] featured a database with an equal distribution of cases and controls (ration 123 : 117), and found that primiparous women and those with pre-eclampsia had a significantly ($p < 0.01$) greater risk of a low Apgar score. A study by Chiabi et al. [3] found the following antepartum risk factors: place of antenatal visit, malaria during pregnancy, and preeclampsia. Intrapartum risks included: prolonged labor, stationary labor, and term prolonged rupture of membranes. A study from Uganda on antenatal and intrapartum risks by Kaye [8] reported anemia, pre-eclampsia, meconium stained fluid and low birth weight among the most significant risks with respect to outcome assessed by the Apgar score. In an interesting work of Landfors [9] meconium was highlighted together with several CTG-related parameters as the factors increasing the risk of asphyxia (again assessed based on Apgar score) the most.

In our previous work we have focused on evaluations of CTG recordings and their relation to pH c.f. [4,15], and on evaluation of decision-making processes of expert obstetricians [21] using the CTG recording database available at the University Hospital in Brno [5]. Since year 2014 we have also been collecting structured clinical data on all deliveries. Preliminary results of our analysis are presented bellow.

2 Methods

Our study is a data-driven retrospective exploratory analysis utilizing the University Hospital in Brno database consisting of clinical data as well as the CTG recordings, which are in part published as an open-access database [5]. After a previous attempt to understand in depth the individual relations in the data [11] we focus here on a detailed univariate analysis of the collected features.

2.1 Database

The data were collected using our own data collection system, DeliveryBook, at the delivery ward of the University Hospital in Brno from January 2014 to December 2015. More than 100 clinically relevant parameters about mother, delivery and newborn are stored in a structured way. The collection and use of the data was approved by the ethics committee at the University Hospital in Brno. All data are fully anonymized. The database consists of 12274 recordings, but in order to allow straightforward interpretation we have used the following conditions in order to homogenize the final set: arterial pH is available; gestational age $\leq$37 weeks; singleton pregnancy; no known congenital diseases. This yielded in total 10637 deliveries for analysis.

Table 1. A collection of the most interesting results from a univariate analysis of the features. pH, Apgar and SC are outcome measures, while all the other features represent knowledge or an action known prior to delivery. Entonox and epidural analgesia are medications given during the labor.

	Cases – $pH \leq 7.05$			Controls – $pH > 7.05$				
	#	prct (%)	mean (std)	#	prct (%)	mean (std)	OR (95 % CI)	p-value
pH ≤ 7.05	99	0.93	6.99 (0.09)	10523	99.07	7.29 (0.08)	-	-
Apgar score 5 min	203	1.91	6.50 (0.88)	10400	98.09	9.65 (0.59)	24.68 (15.49 - 39.31)	<0.001
Sectio Caesarea	2110	20.30	1.00 (-)	8285	79.70	0.00 (-)	1.58 (1.02 - 2.45)	<0.001
Induced delivery	2198	20.69	1.00 (-)	8424	79.30	0.00 (-)	1.44 (0.92 - 2.25)	<0.001
Entonox	144	1.36	1.00 (-)	10478	98.64	0.00 (-)	2.30 (0.72 - 7.35)	<0.001
Epidural analgesia	1915	18.03	1.00 (-)	8707	81.97	0.00 (-)	1.01 (0.60 - 1.69)	1.000
Ist stage (> 360 min)	1807	18.40	440.15 (64.77)	8015	81.60	226.22 (73.79)	1.36 (0.84 - 2.20)	<0.001
IInd stage (> 30 min)	884	10.11	54.12 (20.60)	7862	89.89	11.04 (7.18)	2.86 (1.70 - 4.81)	<0.001
Parity (< 2)	5299	49.99	1.00 (0.00)	5302	50.01	2.34 (0.78)	2.99 (1.90 - 4.71)	<0.001
Sex (Male)	5468	51.53	1.00 (-)	5143	48.47	2.00 (-)	0.69 (0.46 - 1.03)	0.001
O100 – hypertension	533	5.02	-	10089	94.98	-	1.45 (0.67 - 3.13)	<0.001
O140 – preeclampsia	114	1.07	-	10508	98.93	-	1.92 (0.47 - 7.87)	0.008
O365 – IUGR	375	3.53	-	10247	96.47	-	1.78 (0.77 - 4.08)	<0.001
O681 – meconium	784	7.38	-	9838	92.62	-	2.09 (1.18 - 3.69)	<0.001
D650 – defibrination syndrome	258	2.43	-	10364	97.57	-	2.63 (1.14 - 6.06)	<0.001
D695 – secondary thrombocy-topenia	36	0.34	-	10586	99.66	-	6.36 (1.51 - 26.85)	<0.001

2.2 Features

A total of 107 features were analysed all of them falling into one of the following categories: (a) detected prior to going into labour (e.g. parity, sex of the fetus, induction of labour, some diagnosis related to mother and pregnancy) (b) occurring within the delivery period (e.g. interventions, length of delivery stages, medications, diagnosis related to delivery) (c) features known after delivery – outcome measures (e.g. Apgar score, admittance to the NICU, seizures or intubation).

2.3 Statistical Evaluation

The relation between each feature and the pH outcome was evaluated using univariate logistic regression to obtain odds ratios, their 95 % confidence intervals (CI), and two-sided p-values, in addition to basic descriptive statistics.

An odds ratio (OR) is a measure of the association between an exposure and an outcome. It answers the question - how much of a difference does the presence of the risk factor have on your chances of getting the disease [14]? Odds ratios are most commonly used in case-control studies. However they can also be used in cross-sectional and cohort study designs [17]. Additional information on the OR can be found in the statistical notes by Bland [2], with arguments supporting the OR over relative risk (RR) estimation. In our case, the difference between OR and RR is anyway negligible, since the event rate of pathological cases is very low, so $OR \simeq RR$ [14]. All computations were done in Matlab 2015a.

3 Results

All results are shown in Table 1. The main parameter defining the two groups (cases and controls) of newborns was the umbilical artery pH (set to 7.05) – a common set-up value in the studies using pH c.f. e.g. [20,22].

4 Discussion

Several features related to low pH outcomes were identified. However some uncertainties on the side of the database and the interpretation of the results will have to be clarified before we move on to the multivariate analysis.

First, although the size of the database is promising, the main concern is the size of the subsets representing individual features. Especially for diagnostic features where ICD-10 codes are used, many subsets contain only tens of cases, which is insufficient to allow conclusions to be drawn with high confidence.

Second, although all features, with the exception of epidural analgesia, are deemed significant with $p < 0.01$, it is necessary to interpret carefully the clinical relevance of all OR that span over $OR = 1$.

According to our review of the available literature, no studies have related the clinical features known before and during delivery to the outcome in the form of the pH value. Although some studies e.g. by Dani [6] suggest the link between low pH and an adverse outcome is only weak, there are other studies, e.g. by Yeh [19] showing a significant increase in the risk of neurological impairment with $pH \leq 7.1$. Thus, irrespective of the controversy surrounding pH as an outcome measure it should be an imperative to avoid a low pH value.

Our study highlights features related to low pH. Although many of the parameters are known to increase the risk for the baby our data driven analysis gives additional evidence with respect to low pH.

The ultimate goal in utilizing data available from the database is to marry the clinical data analysis with CTG/FHR analysis in order to provide comprehensive decision support during delivery. The study presented here is just an initial investigation into the database.

5 Conclusion

An analysis of risk factors for low umbilical cord artery pH was undertaken and identified several interesting features related to parity, sex of the fetus, induced labour, and also those related to specific diagnosis codes related with the delivery – e.g. meconium staining (O681) and defibrination syndrome (D650).

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References

1. Aslam, H.M., Saleem, S., Afzal, R., Iqbal, U., Saleem, S.M., Shaikh, M.W.A., Shahid, N.: Risk factors of birth asphyxia. Ital. J. Pediatr. **40**(1), 1–9 (2014)
2. Bland, J.M., Altman, D.G.: Statistics notes. The odds ratio. BMJ **320**(7247), 1468 (2000)
3. Chiabi, A., Nguefack, S., Evelyne, M., Nodem, S., Mbuagbaw, L., Mbonda, E., Tchokoteu, P.-F., Anderson, D.: Risk factors for birth asphyxia in an urban health facility in cameroon. Iran. J. Child Neurol. **7**(3), 46–54 (2013)
4. Chudáček, V., Spilka, J., Huptych, M., Georgoulas, G., Lhotská, L., Stylios, M., Koucký, C., Janků, P.: Linear and non-linear features for intrapartum cardiotocography evaluation. In: Computers in Cardiology, vol. 35 (2010)
5. Chudáček, V., Spilka, J., Burša, M., Janků, P., Hruban, L., Huptych, M., Lhotská, L.: Open access intrapartum CTG database. BMC Pregnancy Childbirth **14**(1), 16 (2014)
6. Dani, C., Bresci, C., Berti, E., Lori, S., Di Tommaso, M., Pratesi, S.: Short term outcome of term newborns with unexpected umbilical cord arterial pH between 7.000 and 7.100. Early Hum. Dev. **89**(12), 1037–1040 (2013)
7. Gareen, I.F., Morgenstern, H., Greenland, S., Gifford, D.S.: Explaining the association of maternal age with cesarean delivery for nulliparous and parous women. J. Clin. Epidemiol. **56**(11), 1100–1110 (2003)
8. Kaye, D.: Antenatal and intrapartum risk factors for birth asphyxia among emergency obstetric referrals in mulago hospital, kampala, uganda. East Afr. Med. J. **80**(3), 140–143 (2004)
9. Ladfors, L., Thiringer, K., Niklasson, A., Odeback, A., Thornberg, E.: 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. **81**(10), 909–917 (2002)
10. Leuthner, S.R., et al.: Low apgar scores and the definition of birth asphyxia. Pediatr. Clin. North Am. **51**(3), 737–745 (2004)
11. Burša, M., Lhotská, L., Chudáček, V., Spilka, J., Janků, P., Hruban, L.: Information retrieval from hospital information system: increasing effectivity using swarm intelligence. J. Appl. Logic **13**(2), 126–137 (2015)

12. Martius, J.A., Steck, T., Oehler, M.K., Wulf, K.H.: Risk factors associated with preterm (< 37+ 0 weeks) and earlypreterm birth (< 32 + 0 weeks): univariate and multivariate analysis of 106345 singleton births from the 1994 statewide perinatal survey of bavaria. Eur. J. Obstet. Gynecol. Reprod. Biol. **80**(2), 183–189 (1998)
13. Patel, R.R., Peters, T.J., Murphy, D.J., ALSPAC Study Team, et al.: Prenatal risk factors for caesarean section. Analyses of the ALSPAC cohort of 12 944 women in england. Int. J. Epidemiol. 34(2), 353–367 (2005)
14. Schmidt, C.O., Kohlmann, T.: When to use the odds ratio or the relative risk? Int. J. Publ. Health **53**(3), 165–167 (2008)
15. Spilka, J., Chudáček, V., Janků, P., Hruban, L., Burša, M., Huptych, M., Zach, L., Lhotská, L.: Analysis of obstetricians' decision making on CTG recordings. J. Biomed. Inform. **51**, 72–79 (2014)
16. Szal, S.E., Croughan-Minihane, M.S., Kilpatrick, S.J.: Effect of magnesium prophylaxis and preeclampsia on the duration of labor. Am. J. Obstet. Gynecol. **180**(6), 1475–1479 (1999)
17. Szumilas, M.: Explaining odds ratios. J. Can. Acad. Child Adolesc. Psychiatry **19**, 227–229 (2010)
18. Verhoeven, C.J., van Uytrecht, C.T., Porath, M.M., Mol, B.W.J.: Risk factors for cesarean delivery following labor induction in multiparous women. J. Pregnancy **2013** (2013). http://dx.doi.org/10.1155/2013/820892
19. Yeh, P., Emary, K., Impey, L.: The relationship between umbilical cord arterial pH and serious adverse neonatal outcome: analysis of 51,519 consecutive validated samples. BJOG **119**(7), 824–831 (2012)
20. Doret, M., Spilka, J., Chudáček, V., Gonçalves, P., Abry, P.: Fractal analysis and hurst parameter for intrapartum fetal heart rate variability analysis: a versatile alternative to frequency bands and LF/HF ratio. PLoS ONE **10**(8), e0136661 (2015)
21. Hruban, L., Spilka, J., Chudáček, V., Janků, P., Huptych, M., et al.: Agreement on CTG intrapartum recordings between expert-obstetricians. J. Eval. Clin. Pract. **21**(4), 694–702 (2015)
22. Karvelis, P., Spilka, J., Georgoulas, G., Chudáček, V., Stylios, C.D., Lhotská, L.: Combining latent class analysis labeling with multiclass approach for fetal heart rate categorization. Physiol. Meas. **36**(5), 1001–1024 (2015)