Maternal risk factors for "adverse neonatal outcome" after term deliveries in Sri Lanka.

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Abstract:

Background:

Even though forty to seventy percent of neonatal mortality are recorded among term neonates, information on neonatal outcomes of term neonates is scarce. The high volume of term neonatal admissions to neonatal care units(NCU)signifies the importance of studying the maternal risk factors for such neonatal outcomes.

Objectives:

The present study aims to identify the maternal risk factors for' "adverse neonatal outcome" (ANO) following term deliveries at Teaching Hospital Kandy.

Methods:

An unmatched case-control study was nested within a descriptive follow-up study. A sample of 1105 neonates, delivered at term at Teaching Hospital Kandy, was followed up until their initial discharge point.

Results:

Multivariate analysis, found that caesarean section with labour increases the risk of ANO among term neonates by 3.37 (CI- 2.13-5.33) times compared to normal vaginal delivery. Further, 37 completed weeks of Period of Amenorrhea (POA) (OR-2.91,1.57-5.42), Pregnancy Induced Hypertension (PIH) (OR-2.46, CI- 1.27-4.75), Gestational Diabetes Mellitus (GDM) (OR-2.33, CI- 1.0-5.15), primiparity (OR-1.53, CI- 1.02-2.30) and maternal occupation as professionals (OR-3.45, CI- 1.46-8.13) was identified as independent risk factors of ANO among term neonates.

Conclusions:

Caesarean section with labour, 37 completed weeks of POA, PIH, GDM, primiparity and maternal occupation as professional are independent risk factors for ANO in term neonates.

Keywords: Term neonate, adverse neonatal outcome, maternal risk factors

Introduction:

Sri Lanka has reduced the infant mortality rate from 17.7 in 1991 to 9.4 in 2009, with a neonatal mortality rate of 5.9 in 2009. However, neonatal deaths account for more than 80 percent of infant deaths. Therefore, further reduction in infant mortality will only be possible through improving newborn health. Significant causes of neonatal mortality in

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Sri Lanka are prematurity, congenital anomalies, birth asphyxia, neonatal sepsis, meconium aspiration syndrome. $^{\rm 1}$

When all neonatal deaths are considered, 40-70% of neonatal deaths are among term neonates. ² Even though the neonatal outcomes of preterm neonates have been extensively studied, information on neonatal outcomes at term is scarce. The high volume of term neonatal admissions NCUs further signifies the importance of studying the risk factors for adverse neonatal outcomes among term neonates.

When conducting studies among neonates, different methodologies have been used to assess adverse outcomes. A follow-up study done by Tita et al. ³ used a pre-specified composite outcome as the primary outcome, including death, adverse respiratory outcomes, hypoglycemia, etc. Few other studies ^{4,5} focused on adverse outcomes among term neonates used neonatal intensive care admission as their primary outcome to assess associated risk factors.



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Various maternal factors related to adverse neonatal outcomes such as low birth weight, prematurity have been studied extensively. However, studies done on term neonates to identify maternal risk factors for adverse outcomes are not many.

Adverse sociodemographic factors are well proven to result in poor maternal and neonatal outcomes. Extremes of maternal age, teenagers and elderly mothers, mothers from poor socioeconomic backgrounds, women employed in unskilled labour are known to have poor outcomes at childbirth.

Olusanya et al. ⁶ studied the outcome of term babies considering admission to a special care baby unit as a proxy of adverse outcome and found that first-born babies and babies of women employed in unskilled manual labour had higher admission rates to the neonatal units.

In a matched-paircase-control study⁷ with full-term low birth weight babies (n=274), maternal height < 145 cm, pre-delivery weight < 55kg, pregnancy weight gain 6 kg, and maternal anaemia were found to be associated with the delivery of term low birth weight neonate.

Mumbare, et al. ⁷reported inadequate antenatal care as a significant predictor for delivering a low-birthweight baby at term.

A telephone survey done by Rose et al. 8 to determine the maternal factors associated with neonatal intensive care admissions found that multiple gestations, preterm, premature rupture of membranes, diabetes, abruption placentae, pregnancy induced hypertension are independently associated with at least a 3 fold risk of neonatal intensive care unit admission.

A cross-sectional study9conducted to identify risk factors for birth asphyxia at term found hypertension, toxaemias of pregnancy, antepartum haemorrhage, prolonged rupture of membranes are significantly associated with birth asphyxia.

As revealed by Sharma et al. 10, the mode of delivery directly impacts the neonatal outcome. Caesarean section and operative vaginal and breech vaginal delivery carry significant neonatal risk. At the same time, forceps assisted delivery has a higher risk of neonatal death than vacuum-assisted delivery. Even though there is a concern about rising rates of caesarian delivery throughout the world, the increasing trend continues in many countries¹¹. Caesarean sections independently reduce overall risk in breech deliveries but increase the risk of neonatal morbidity and mortality in cephalic presentation¹¹.

A study done to ascertain intrapartum risk factors for term neonates who have ventilation found several maternal risk factors for the conditions, including gestational age 37-38 weeks, inducedlabour, forceps delivery, elective and emergency caesarean section^{12,13}

Almost 90% of the babies are born at term in Sri Lanka1. Therefore, it would be beneficial to conduct a study to identify maternal risk factors for adverse neonatal outcomes at term, signify the importance of prevention and management of adverse neonatal outcomes among term neonates.

Therefore, this study aims to identify maternal risk factors for "adverse neonatal outcome" following term deliveries at Teaching Hospital Kandy.

Methods:

This study was designed as an Unmatched casecontrol study, nested within a descriptive follow-up study, conducted at Teaching Hospital Kandy for three months from 26th of February to 20th of May 2015. A sample of 1105 neonates delivered at term were followed up until their initial discharge point. This study was approved by the ethical review committee of Faculty of Medicine, Colombo.

Cases were defined as term neonates with "adverse neonatal outcome" (ANO), a composite measure of neonatal death and morbidity that needed admission to a neonatal care unit before the initial hospital discharge point. Controls were defined as term neonates who were alive and did not require admission to a NCU until the initial discharge point.

Sample size calculation had been performed to explore the adequacy of the cases and controls. In the sample size calculation investigator assumed the prevalence of the various risk factors among the control group to be in the range of 12.1-67% ^{4,12} based on available published data. With low prevalence (10-15%) of outcome, a 1:3 ratio between cases and controls was taken to increase the power. Hence with an assumed exposure rate of 10% and to detect an odds ratio of at least 2 with a power of 80% at a significance level of 5%, principal investigator, calculated a sample size of 165 cases and 493 controls to be used in the study. Therefore all the 175 neonates with ANO in the database were selected as cases, and a random sample of 525 neonates was selected out of 930 neonates without ANO as controls. This control selection was made through the SPSS software.

Term delivery defined in the original study as delivery occurred during the period of gestation from 37 completed weeks (259days) up to and including 41 completed weeks and 6 days (293days), based on the gestational age at delivery. In the follow-up study following term neonates were excluded from the study; neonates of mothers with uncertain Last Menstrual Period (LMP), neonates of mothers who did not have an ultrasound scan (USS) before the completion of 24 weeks of gestation and neonates of mothers whose USS Expected Date of Delivery (EDD) is different from EDD calculated by the LMP more than 14 days.

Maternal risk factors considered in this study included risk factors related to sociodemographic characteristics, biological characteristics and obstetric characteristics of mothers, namely; maternal age (in completed years), height (as recorded in the maternal record), pre-pregnancy weight (as recorded in the maternal record during 1st trimester), Body Mass Index (BMI), Pregnancy weight gain, education level, occupational status, monthly income of the family, past illness, parity, interpregnancy interval, Risk conditions during past pregnancies, PIH, GDM, Vaginal bleeding during pregnancy, intrauterine growth restriction, maternal anaemia, POA at delivery, labour onset and mode of delivery. Categorisation of variables such as maternal age, height, pre-pregnancy weight, pregnancy weight gain and inter-pregnancy interval had been done based on the risk factors identified in the previous studies. BMI and adequacy of pregnancy weight gain were categorised according to the maternal care guideline in Sri Lanka. 14Self-reported highest educational attainment and occupation was classified according to the classifications used by the department of census and statistics in Sri Lanka. 15 Parity was classified as primipara (women who had never given birth one time) and multipara (women who had given birth one or more times).

The onset of labour was classified into three groups; spontaneous, induced and no labour based on the mode of initiation of the labour. Interpregnancy interval was calculated as the time between previous birth and the beginning (conception) of the present pregnancy in completed months. POA was measured in completed weeks of gestation. Attending the antenatal clinic after 16 weeks of POA or less than 50 percent of recommended antenatal clinic visits was defined as inadequate antenatal care.

Bivariate logistic regression was performed to determine the association between each independent variable and "adverse neonatal outcome". Odds ratios and the 95 percent confidence intervals were

determined. A two-tailed probability of < 0.05 was considered significant.

Multivariate analysis was performed to control for the confounding factors. The variables that gave the probability of less than 0.25 from the bivariate analysis were included in the multivariate logistic regression model for the primary outcome. Even if one category had a p-value less than 0.25, variables had been selected for the multivariate model in the variable selection.

Likelihood ratio test p-value had been used to add or delete independent variables in the model. Values of the estimated coefficients were compared between smaller and larger models in deleting variables to identify possible confounding variables. In particular, a 20 percent change in the magnitude of the estimated coefficient was used as the criteria for detecting confounding. The goodness of the fit of the model was assessed through Hosmer and Lemeshow test. From the final model, the adjusted odds ratios and the 95 percent confidence intervals were derived for each of the levels of risk factor variables.

Data processing, including categorisation of variables and labelling, had been done in the SPSS 22nd version. But both bivariate and multivariate analysis were performed with the Minitab 17th version.

Out of all term neonates, 15.84% (n=175) were admitted to the NCU, and 23.3% (n=257) had at least one diagnosed neonatal condition. In the univariate analysis (Table 1), mothers with pre-pregnancy weight 45kg or less were more likely to have "adverse neonatal outcomes" than their counterparts. When focused on pre-pregnancyBMI, underweight mothers had only about half of the risk (OR 0.48, CI 0.30-0.80) of ANO compared to normal BMI mothers who delivered term neonates. Term neonates of mothers who had undergone induction of labour had a 1.98 times higher chance of developing "adverse neonatal outcome". However, none of the pregnancy weight gain categories was associated with ANO at term. Further, pregnancy weight gains less than 6 Kg also not associated with ANO among term neonates.

Table 1 Maternal risk factors for "adverse neonatal outcomes" univariate analysis results

Maternal Age	Case	s	Controls		OR	СІ	Р
<20	3	1.7	27	5.1	0.33	0.1-1.10	0.070
20 to 35	142	81.1	419	79.8	Reference		
> 35	30	17.1	79	15.0	3.42	0.97-	0.630
Height (cm)							
145 or less	18	10.3	42	8.0	1.32	0.74-2.36	0.35
>145	157	89.7	483	92.0	Reference		
Weight (Kg)							
45 or less	35	20.1	162	32.0	0.54	0.35-0.81	0.003
>45	139	79.9	344	68.6	Reference		
(Missing)	(1)		(19)				
Body Mass Index (BMI)(Kg/m²)							
<18.5	24	13.8	133	26.3	0.48	0.30-0.80	0.004
18.5-24.99	100	57.5	269	53.2	Reference		
25.0-29.99	40	23.0	83	16.4	1.296	0.83-2.02	0.249
30.00 or more	10	5.7	21	4.2	1.281	0.58-2.8	0.538
(Missing)	(1)		(19)				
Pregnancy Weight Gain Category							
Not adequate	96	57.8	282	56.6	1.01	0.67-1.49	0.976
Adequate	50	30.12	146	29.32	Reference		
More than adequate	20	12.05	70	14.06	0.84	0.48-1.45	0.531
Pregnancy weight gain(Kg)							
<6Kg	33	19.88	74	14.86	1.42	0.90-2.24	0.129
6 or more	133	80.12	424	85.14	Reference		
Total	166	100.0	498	100.0			
Education Level							
Below GCE O/L	98	18.7	29	16.6	082	0.51-1.3	0.437
GCE O/L Pass	220	41.9	79	45.1	Reference		
GCE A/L Pass	168	32.0	59	33.7	0.98	0.66-1.45	0.912
Degree or above	39	7.4	8	4.6	0.57	0.26-1.28	0.172
Occupational Status							
Professionals	12	6.9	19	3.6	2.00	0.97-4.32	0.06
Clerks	11	6.3	30	5.7	1.18	0.58-2.43	0.640
Other	17	9.7	39	7.4	1.41	0.77-2.58	0.26
House wife	135	77.1	437	832	Reference		
Monthly Family Income (Rs.)	n	%	n	%			
<15000.00	27	15.4	84	16.0	1.00	0.54-1.85	1.00
15000.00 - 30000.00	84	48.0	249	47.4	1.05	0.64-1.73	0.849
30001.00- 45000.00	37	21.1	108	20.6	1.07	0.60-1.89	0.827
More than 45000.00	27	15.4	84	16.0	Reference		

Past illness	n	%	n	%			
Yes	38	21.7	86	16.4	0.84	0.59-1.19	0.32
No	137	78.3	439	83.6	Reference		
Parity	n	%	n	%			
Pirmi parity	90	51.4	217	41.3	1.50	1.07-2.12	0.02
Multiparity	85	48.6	308	58.7	Reference		
Interpregnancy Interval (Months)							
<24	10	12.0	53	17.3	1.57	0.74-3.33	0.24
24-59	45	49.5	152	49.5	Reference		
60 or above	28	33.7	102	33.2	1.07	0.63-1.84	0.78
Risk conditions during past pregnancies	n	%	n	%	1.07	0.00 1.01	0.70
Yes	44	51.8	180	58.4	0.76	0.47-1.24	0.272
No	41	42.2	128	41.6	Reference	0.47-1.24	0.272
Antenatal care	71	42.2	120	41.0	Reference		
Not Adequate	63	36.0	180	34.3	0.928	0.65-1.33	0.68
•	112	64.0	345	65.7	Reference	0.03-1.33	0.08
Adequate Antenatal Complication		%		%	Reference		
·	n	70	n	70			
Pregnancy Induced Hypertension	24	12.0	22	6.1	2.10	1.18-3.75	0.11
Yes	21		32	6.1		1.18-3.75	0.11
No	154	88.0	493	93.9	Reference		
Gestational Diabetes	4-	0.5	4.5		2.00		
Yes	15	8.6	16	3.0	2.98	1.44-6.16	0.002
No	160	91.4	509	97.0	Reference		
Vaginal bleeding during antenatal							
Yes	5	2.9	17	3.2	0.88	0.32-2.42	0.802
No	170	97.1	508	96.8	Reference		
Intra Uterine Growth Restriction							
Yes	4	2.3	8	1.5	1.512	0.45-5.08	0.50
No	171	97.7	517	98.5	Reference		
Maternal Anaemia	n	%	n	%			
Yes	33	18.9	137	26.1	0.66	0.43-1.01	0.053
No	142	81.1	388	73.9	Reference		
POA at Delivery (Weeks)	n	%	n	%			
37	43	24.6	62	11.8	2.55	1.46-4.44	0.001
38	43	24.6	155	29.5	1.02	0.60-1.72	0.94
39	31	17.7	114	21.7	Reference		
40	56	32.0	163	31.0	1.26	0.77-2.08	0.359
41	2	1.1	31	5.9	0.24	0.05-1.05	0.057
Labour onset	n	%	n	%			
Spontaneous	89	50.9	304	57.9	Reference		
Induced	44	25.1	76	14.5	1.98	1.27-3.07	0.002
No labour	42	24.0	145	27.6	0.99	0.65-1.50	0.960
Mode of delivery					0-6		
Mode of delivery Normal Vaginal	74	42.3	302	57.5	Reference		
	74 57	42.3 32.6	302 73	13.9	3.19	2.07-4.90	0.001
Normal Vaginal			-			2.07-4.90 0.31-8.58	0.001 0.56
Normal Vaginal CS with labour	57	32.6	73	13.9	3.19		

Table 2 Maternal risk factors for "adverse neonatal outcomes", multivariate analysis

Variables	OR	95 %CI	P
Mode of delivery			0.001*
Normal Vaginal Delivery	Reference		
CS with labour	3.37	2.13-5.33	0.001
Instrumental	2.21	0.34-14.19	0.401
CS without labour	0.841	0.52-1.39	0.508
POA at birth (Weeks)			0.001*
37	2.91	1.57-5.42	0.001
38	1.10	0.62-1.97	0.730
39	Reference		
40	1.23	0.71-2.09	0.452
41	0.22	0.05-1.03	0.055
Pregnancy Induced Hypertension			0.009*
No	Reference		
Yes	2.46	1.27-4.75	0.007
Gestational Diabetes			0.038*
No	Reference		
Yes	2.33	1.06-5.15	0.035
Maternal Education			0.007*
GCE O/L Pass	Reference		
Below GCE O/L	0.87	0.51-1.48	0.611
GCE A/L Pass	0.80	0.51-1.24	0.328
Degree or above	0.19	0.07-0.514	0.001
Mother's occupation			0.034*
Housewife	Reference		
Clerks	1.96	0.79-4.84	0.146
Other	1.32	0.68-2.52	0.404
Professionals	3.45	1.46-8.13	0.005
Mother's age			0.010*
<20	0.19	0.053-0.69	0.012
20-35	Reference		
>35	1.20	0.69-2.06	0.504
Parity			0.038*
Primi parity	1.53	1.02-2.30	0.039
Multi-Parity	Reference		

^{*}P-value of the variable in likely-hood ratio test

CS - Caesarean Section

These included maternal age, BMI, the level of education, maternal occupation, parity, -inter-pregnancy interval, PIH, GDM, maternal anaemia, pregnancy weight gain, POA at birth, the onset of labour, and mode of delivery.

The final multivariate analysis was performed, taking into account the biological knowledge about independent variables and how they relate to the adverse neonatal outcome. Under multivariate analysis, it was found that caesarean section with labour increases the risk of ANO among term neonates by 3.37 (CI- 2.13-5.33) times compared to normal vaginal delivery. 37 completed weeks of POA (OR-2.91, 1.57-5.42), PIH (OR-2.46, CI-1.27-4.75) Gestational diabetes (OR-2.33, CI- 1.06-5.15) , parity (OR-1.53, CI- 1.02-2.30) and maternal occupation as professionals (OR-3.45, CI- 1.46-8.13) was identify as independent risk factors of 'adverse neonatal outcome' among term neonates. Maternal age < 20 (OR-0.19, CI- 0.053-0.69) and degree or above maternal education level (OR-0.19, CI- 0.07-0.514) were found to be protective factors against the primary outcome of the study. These findings are summarised in "Table 2".

Discussion:

Multivariate analysis showed that maternal age less than 20 years was a protective factor for the study's primary outcome. But this could be due to the fact that teenage mothers are at higher risk of preterm delivery. Therefore, the subsample of teenage mothers in this study might not be representative of the true teenage mother's population.

In contrast to our study findings, Sutton, et al. 12 reported maternal age 35 or more as an independent risk factor for infants ventilated primarily for lung disease among singleton term neonates. On the other hand, Olusanya 6 used a similar age classification as in the present study and found no significant association between maternal age and special care baby unit (SCBU) admissions among full-term normal birth weight babies in Nigeria.

When considering the pre-pregnancyBMI, underweight mothers had only about half of the risk (OR 0.48, CI 0.30-0.80) of ANO compared to normal BMI mothers who delivered term neonates in the bivariate analysis. But this could be due to the confounding effect of maternal age on BMI because nearly half of the teenage mothers were underweight. In the present study, overweight and obesity were not associated with the ANO at term. Pregnancy weight gains less than 6 Kg were not associated with ANO among term neonates in the present study, as

shown in a previous study 7.

Multivariate analysis showed that maternal educational level of degree or above as a protective factor (OR-0.19, CI- 0.07-0.51) for the ANO among term neonates. In agreement with our finding Mumbare, et al. 7 reported a significant association between low maternal education and the term low birth weight in bivariate analysis but not in the multivariate model. This could be due to the relationship between educational level and health literacy. Other studies that have been referred did not report any significant association between maternal educational level and the adverse neonatal outcomes at term. ^{6,9}

When considering the mother's occupational status, professionals (OR-3.45, CI-1.46-8.13) had a higher risk of ANO at term in the multivariate analysis. This could be due to a low threshold for admitting term neonates of professionals, including health care professionals.

More than half of mothers of neonates with ANO in the present study were prim- parous mothers. The risk of ANO in prime mothers was about one and half times (OR-1.53, CI- 1.02-2.30) more than that of multiparity mothers in multivariate analysis. Similarly, Olusanya 6 reported primiparity as a risk factor for SCBU admissions among term normalweight babies. This may be due to low awareness of antenatal and postnatal care among primiparity mothers than the multiparty mother, as suggested by Babu et al. 9

In the present study, no association had been found between inadequate antenatal care and ANO among term neonates in either bivariate or multivariate analysis in the present study. In contrast, Olusanya ⁶ and Mumbare, et al. ⁷ reported a significant association between inadequate antenatal care and adverse outcomes among term neonates. Olusanya 6 defined inadequate antenatal care as not attending antenatal clinics and Mumbare, et al. ⁷ considered antenatal care as inadequate when the pregnant woman had less than three antenatal check-ups. If these definitions were adopted in the present study, the proportion of mothers with inadequate antenatal care would be negligible due to very high antenatal coverage in Sri Lanka.

Out of 119 mothers with at least one antenatal complication (except anaemia) during present pregnancy, 44.54 percent had PIH, followed by GDM (26.05%), vaginal bleeding during the antenatal period (18.49%) and Intra Uterine Growth Restriction (IUGR)(10.08%). Out of these, PIH (OR-2.46,

CI- 1.27-4.75) and GDM (OR-2.33, CI- 1.06-5.15) were found to be associated with ANO among term neonates in our study. Similarly, PIH and GDM both identified as risk factors in previous studies done among term neonates regarding adverse outcomes. 6,7,9,12 Early diagnosis and treatment of both these conditions should be ensured by strengthening the implementation of guidelines given with regard to the national maternal care package in Sri Lanka. 14

Maternal anaemia has been considered a separate entity among antenatal complications developed during pregnancy since it could be developed during pregnancy or pre-existing. Maternal anaemia (Hb < 11.00 g/dl) seems to be a protective factor against the primary outcome of our study. But this associationwere not significant either in bivariate or multivariate analysis. This could be due to the association between maternal anaemia and low birth weight, and thereby reduce the risk of caesarian section with labour.

When considering the POA at birth, delivery at 37 weeks (OR-2.91, CI- 1.57-5.42) was significantly associated with ANO among term neonates. This finding accords with a population-based study done in Australia, which reported, irrespective of the mode of delivery, deliveries that occurred at the 37 weeks had the highest risk of NICU admission at term, followed by 41 and 38 weeks. Furthermore, Sutton, et al. 12 reported a significant association between deliveries occurring at 37 or 38 weeks and NICU admissions among term neonates. In the present study, 23.5% of labour inductions and 66.7% of elective sections were done at 37 or 38 weeks. All these findings signify the importance of preventing any non-medically indicated elective inductions or caesarean sections at 37 weeks of POA.

In the present study, induction of labour (OR-1.98, CI- 1.27-3.07) was a significant risk factor for the ANO among term neonates in the bivariate analysis. This finding accords with those of Sutton, et al. ¹³

With regard to the mode of the delivery, caesarean section with labour (OR-3.37, CI- 2.13-5.33) was found to be associated with ANO at term compared to normal vaginal delivery in the present study. A similar finding has been reported by Tracy, et al. 5, where the highest risk of NICU admission of term neonates was noted among caesarian sections with labour at 40 weeks of POA. This signifies the importance of delaying the elective inductions until the 41 weeks of POA since the caesarean section following failed inductions will considerably increase the risk of ANO at term.

Conclusions

The cesarian section with labour, 37 completed weeks of POA at delivery, PIH, GDM, primiparity and maternal occupation as professionals are independent risk factors for ANO in term neonates. On the other hand, the educational level of degree or above was found to be a protective factor for ANO in term neonates.

Based on our study findings, implementation of the national guideline on induction of labour is strongly recommended. Induction of labour is recommended for low-risk women who are known with certainty to have reached 41 weeks of gestation since caesarean section with labour is identified as a very strong risk factor for ANO among term neonates. Further, any non-medically indicated elective deliveries at 37 weeks should be avoided. A clinical auditing system and a review mechanism should be developed to routinely monitor the indications and outcomes regarding induction of labour and caesarean sections.

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