Original Research

Risk factors of preterm birth in Sri Lanka: case-control study

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Abstract

Introduction: Preterm birth is a major challenge as a contributor to neonatal and child mortality in low- and middle-income countries (LMIC). Many countries toil to prevent and care for preterm babies. Country-specific solid data on risk factors of preterm births are crucial to formulate preventive strategies.

Objectives: To determine the antenatal risk factors of preterm births in Sri Lanka

Methods: An unmatched case-control study was conducted in seven Government hospitals with obstetric and neonatal care facilities in Colombo District in Sri Lanka. Live-born, spontaneous or provider-initiated, 374 preterm babies (<37 & >24 weeks of gestation) as cases and live-born 374 term babies as controls were recruited from mothers who had a dating scan before 22 weeks. A risk factor profile worked out by extensive literature search and consultation of experts was subjected to multivariable analysis to identify risk factors.

Results: Risk factors identified were: multiple pregnancy (adjusted odds ratio (aOR)=10.57; 95% CI: 3.48, 32.08); bleeding/spotting during pregnancy (aOR=3.51; 95% CI: 1.77, 6.98), past preterm birth (aOR= 2.83; 95% CI: 1.09, 7.36), recent stressful life event (aOR=2.62; 95% CI: 1.43, 4.81), higher gravidity (aOR=2.58; 95% CI: 1.35, 4.9), dissatisfaction with self-assessed own health (aOR=2.54; 95% CI: 1.52, 4.22), pregnancy induced hypertension (aOR=2.25; 95% CI: 1.16, 4.38), no antenatal dental assessment (aOR=2.16; 95% CI: 1.23, 3.81), unsatisfactory oral hygiene (aOR=2.01; 95% CI: 1.33, 3.04), long standing hours during 3rd trimester (aOR=1.91; 95% CI: 1.24, 2.94) and cooking using firewood (aOR=1.51; 95% CI: 1.01, 2.25). Sexual abstinence (aOR=0.46; 95% CI: 0.26, 0.81) was a protective factor.

Conclusions & Recommendations: Modifiable and unmodifiable factors for preterm births were identified. Special care during pregnancy and early admission is recommended for multiple pregnancy, those had spotting during pregnancy and those had past preterm delivery. Avoiding stress during pregnancy and emphasizing oral hygiene are recommended.

Keywords: *preterm birth, risk factors, middle-income country, Sri Lanka*

Introduction

Fifteen million babies are born preterm globally every year reflecting a rising trend (1). Worldwide, for every 10 live births, one baby is born preterm with varying rates of 5-18% between countries (1). A larger proportion (approx. 90%) of preterm births is reported from LMIC (2) with more than 60% from African and Asian countries (1). Sri Lanka is a lower middle-income Asian country with impressive perinatal and infant mortality indices. The country is facing the challenge of service delivery to a substantial number of preterm babies (7.9%) (3) in an annual live birth cohort of 320 000.

The World Health Organization (WHO) defines preterm as babies born before completing 37 weeks or 259 days of gestation (4). Worldwide, health systems face enormous challenges in managing preterm babies. The high number of acute and chronic complications associated with prematurity burden health systems, communities and families. Loaded with a large number of cases and the increasing demand of individualized complex management, preterm birth has become a major contributor to neonatal deaths. The global contribution of preterm births to neonatal mortality shows an increasing trend with 13.7% in 2000 and 17.9% in 2016 (5). In 2015, nearly one million global deaths were due to complications of preterm births (6). A wide disparity prevails between LMIC regarding the survival and quality of life of preterm babies. Out of 10 babies born before 28 weeks of gestation, nine babies die in a low-income country while only one dies in a high-income country within the first few days of life. (7). However, the WHO estimates that more than 75% of preterm lives could be saved with existing cost-effective interventions (7).

Sri Lanka's infant mortality rate has come down to 6 and neonatal mortality to 4 per 1000 live births in 2021 (8). Prematurity is the second leading cause of infant mortality (9). With the wide disparity of survival of preterm babies, many LMIC worldwide scruffle with providing optimal care for them. As a country with an effective preventive health system where every household throughout the country is under the purview of a public health midwife (9), identifying antenatal risk factor profile specific to local settings is a felt need that could lead to formulating targeted preventive strategies. With an estimated preterm caseload of 25 200 (3), Sri Lanka lacks robust preterm data (9). In this background, this study aimed to explore the antenatal risk factors for preterm birth specific to Sri Lanka, and thereby suggest actions to address challenges in reducing preterm births. The outcome of this research would complement the lacuna of evidence especially in LMIC.

Methods

An unmatched multi-centre case-control study was conducted in all government hospitals with obstetric, paediatric and neonatal care facilities in the district of Colombo, Sri Lanka from October 2017 to March 2018. This is the highest populated district in the country, with patients draining from other districts in search of medical care. There were seven hospitals selected for the study; four teaching hospitals and three base hospitals.

The 'Best Obstetric Estimate (BOE)', a standard uniform method advocated by the American College of Obstetricians and Gynaecologists (ACOG) which takes into consideration both the last menstrual period (LMP) and the ultrasonography, was used to identify preterm babies (10-12). The decision to consider LMP date or ultrasound scan date depends on the discrepancy of dates between ultrasound dating and LMP dating. A pretested web-based computer application was used to calculate the POA.

The study population comprised live-born preterm babies who had completed 24 weeks to 36 weeks of gestation as cases; and live-born term babies born at or after 37 weeks of gestation as controls from the

same hospital. Babies with severe congenital abnormalities, birth weight less than 500 g and who had no dating scan before 22 weeks of POA were excluded.

The sample size calculated was 385 in each category of cases and controls, using the formula for case-control studies while taking into consideration a desired probability of type I & II errors of 0.05 and 0.2; 1.8-fold minimum risk, associated with prematurity (13); case to control ratio of 1:1; and 15% non-response. The number of cases recruited from each hospital was proportionate to the deliveries in each hospital in the preceding six months of the study. Both spontaneous and provider-initiated preterm births were included as the objective was to identify antenatal risk factors irrespective of the mode of preterm delivery. The next available live-born babies delivered at term immediately after the index case born in the same hospital were selected as controls.

Several tools were utilized to gather information in the study. An interviewer-administered questionnaire covered essential socio-demographic characteristics of parents and other possible risk factors, such as physical activity, consanguinity, substance abuse, family history of preterm birth, pregnancy preparation by planning, folic acid or subfertility treatment, psycho-social issues such as stress, satisfaction, domestic violence and drug abuse, as well as sexual relationship and environmental characteristics. Physical activity was assessed by the Metabolic Equivalent of Task (MET) value according to the International Physical Activity Questionnaire (IPAQ) (14), while pregnancy planning was assessed using the London Measure of Unplanned Pregnancy (LMUP) questionnaire (15). To assess stressful life events, the Modified Life Events Inventory was adopted, where having at least one event was considered as experiencing a stressful event (16). Satisfaction with one's health was assessed by a five-point Likert scale ranging from totally agree (5-five) to totally disagree (1-one), with scores of 1 to 3 considered as 'unsatisfied' and scores of 4 to 5 considered as 'satisfied' for analysis purposes. Another data extraction sheet was used to extract data directly from the medical records on medical and obstetric histories and current pregnancy status, such as past and present obstetric history, medical illnesses, oral hygiene, and other variables such as maternal anthropometric measurements, related to the antenatal period. Trained pre-intern medical officers collected data at postnatal wards before mother and baby were discharged from the hospital.

Data analysis

A univariable logistic regression was performed to identify unadjusted odds ratio (ORs) of independent variables associated with preterm delivery using the IBM Statistical Package for Social Sciences (SPSS) version 21. Factors significant at the 0.05 level were selected and analysed by multi-variable logistic regression to exclude confounding effects.

Results

The response rate was 97% (374 cases and 374 controls). Babies predominantly belonged to Sinhalese ethnicity reflecting the ethnic composition of the country. There was no significant difference between cases and controls according to the ethnicity or religion of mother or father, their residential health region or sex (Table 1). Most of the cases comprised late preterm babies while only 4% were extremely preterm (Table 2). According to birth weight, one third had normal birth weight while only 5.1% had extremely very low birth weight.

In the univariable analysis (Table 3), 37 factors were significantly associated with preterm delivery. Of them, 12 remained significant in the logistic regression analysis (Table 3) (11 were risk factors and one was a protective factor).

Discussion

Our study identified six modifiable risk factors, namely stressful life events, dissatisfied over own health, no dental assessment, unsatisfactory oral hygiene, longer standing in late pregnancy and use of firewood for cooking. Abstinence from sexual intercourse seven days prior to delivery was identified as a modifiable protective factor. The other five factors could be considered as factors that need extra care. These findings highlight the importance of addressing these factors during the antenatal period to reduce the incidence of preterm births and improve outcomes.

In this study, multiple pregnancy had the highest odds (aOR=10.57) for preterm delivery, which is consistent with previous studies (17-18). Uterine overdistension is believed to be the causative mechanism for the high rate of spontaneous preterm births (19). The higher risk shown in women who had a previous preterm delivery is consistent with previous research (20). It could be hypothesised that the unknown mechanism and factors may persist in subsequent pregnancies.

A stressful life event during the last month of pregnancy had 2.62 times higher risk. This finding was supported by previous research which had used the same modified life events inventory within the country and internationally (16, 20-21).

We found the gravidity of four or more to have 2.58 times higher risk of delivering preterm, compared to those who had gravidity of 3 or less. It has been identified that parity more than 3 among women above 18 years (aOR=1.43) as a risk factor for preterm birth (22). We justify our finding as our sample contained less than 6% of women below the age of 20 years.

Among the psychosocial issues, dissatisfaction over own health had shown 2.54 times higher risk. A study in rural Appalachia in the USA had found that women with symptoms of depression or a negative perception of pregnancy had significantly higher odds of delivering a preterm baby (23). Even if not directly related to the dissatisfaction over own health, it can be considered as almost related, and therefore supports the study finding.

Pregnancy induced hypertension was associated with a 2.25 times higher risk of preterm delivery while a study done in China had shown a similar result with an OR of 6.03 (20). The poor placental perfusion may contribute to preterm birth, but exact mechanisms need to be studied in future research.

It has been postulated that the anaerobic bacteria in dental plaque activate macrophages to secrete cytokines that reach the placenta to accelerate labour (24). Our study found that poor oral hygiene (OR=2.01) and lack of dental check-ups during pregnancy (OR=2.16) increased the risk of preterm delivery. Similar findings were observed internationally (25), emphasizing the importance of dental care and oral hygiene in countries like Sri Lanka with high dental caries prevalence among pregnant women. Addressing this issue before pregnancy and during adolescence is crucial, as treating poor oral hygiene during pregnancy did not mitigate the risk.

Out of all physical activities assessed, the longer standing more than 2.5 hours only during the third trimester (OR=1.91) was significant. This result is confirmed by a systematic review (26). The physical exertion may be causing poor blood supply to the placenta that trigger the labour that leads to preterm birth.

Exposure to firewood cooking smoke during pregnancy increased the risk of preterm delivery by 50% similar to findings from a study in India (27). Foetal growth is weakened by inhaled particulate matter that damage cells through oxidative stress (28). In this context, education on minimizing exposure to wood smoke should be emphasized, especially in the rural community.

Table 1: Place of delivery and basic socio-demographic characteristics of parents of study and control groups

Description	Cases (n=374)		Controls (n=374)		Significance
	No.	%	No.	%	
Ethnicity of mother					
Sinhala	298	79.7	298	79.7	χ^2=1.55*
Tamil	38	10.2	32	8.6	df=3
Muslim	36	9.6	43	11.5	p=0.68
Burger	2	0.5	1	0.3	
Ethnicity of father					
Sinhala	299	79.9	295*	79.3	χ2=2.44*
Tamil	39	10.4	32	8.6	df=3
Muslim	36	9.6	44	11.8	p=0.46
Burger	0	0.0	1	0.3	
Mother's religion					
Buddhist	253	67.6	263	70.3	
Christian	45	12.0	35	9.4	χ2=3.56*
Hindu	39	10.4	33	8.8	df=4
Islam	36	9.6	43	11.5	p=0.47
Not following any religion	1	0.3	0	0.0	
Father's religion					
Buddhist	258	69.0	260*	69.9	
Christian	38	10.2	35	9.4	χ2=1.79*
Hindu	41	11.0	33	8.9	df=4
Islam	36	9.6	42	11.3	p=0.78
Not following any religion	1	0.3	2	0.5	
Residential health region					
Colombo RDHS[$] area	201	53.7	212	56.7	
Colombo Municipal Council area	31	8.3	41	11.0	χ2=7.68
Gampaha	61	16.3	67	17.9	df=4
Kalutara	32	8.6	24	6.4	p=0.1
Other regions (including 15 health regions)	30	8.0	49	13.1	

*Fisher's Exact Test; [#]missing values; [$]Regional Director of Health Services

Abstaining from sexual activity for 7 days in the later stages of pregnancy was protective against preterm birth (OR =0.46) supported by other research as well (20, 29), possibly due to increased uterine pressure, membrane rupture, and prostaglandins in seminal fluids.

Table 2: Distribution of babies according to POA, birth weight and sex

Description	Cases (n=374)		Controls (n=374)	
	No.	%	No.	%
POA category				
Extremely preterm (<28 weeks),	15	4.0		
Very preterm (28 to <32 weeks)	34	9.1		
Moderate preterm (32 to <34 weeks)	44	11.8		
Late preterm (34 to <37 weeks)	281	75.1		
Term			374	100.0
Birth weight category*				
Extremely very low birth weight (<1000 g)	19	5.1	0	0
Very low birth weight (1000 g to <1500 g)	40	10.8	1	0.3
Low birth weight (1500 g to <2500 g)	190	51.1	46	12.3
Normal weight (≥ 2500 g)	123	33.1	327	87.4
Sex of the baby				
Male	191	51.1	195	52.1
Female	182	48.7	178	48.7
Ambiguous	1	0.3	1	0,3

*Missing values in cases

Maternal and paternal age over 35, low maternal education, higher BMI, and unmarried status were not significant factors for preterm birth when adjusted for other variables. However, previous studies have associated these factors with preterm birth. Smoking and HIV prevalence were not assessed due to low prevalence in the study population.

The study excluded preterm babies whose gestational age had not been accurately estimated before 22 weeks of pregnancy and thus, possible psychosocial and medical issues among them may not have reflected in this study. The study focused on identifying risk factors for preterm births and identifying factors that should be monitored during antenatal care at the field level. Due to the non-availability of risk factor data on preterm births at the national level, the study analysed both spontaneous and provider-initiated preterm births together. However, the data collected on antenatal events were subject to recall bias, and efforts were made to facilitate recall by relating to significant events and using average values for measurable variables.

Conclusions & Recommendations

Risk of preterm birth is increased by multiple pregnancy, bleeding/ spotting during pregnancy, history of preterm birth, stressful life event within a month, gravidity of four or more and unsatisfied over own health. Abstinence from sexual intercourse within last seven days is a protective factor. Preventive strategies to reduce preterm birth should focus on modifiable factors and improving the health care quality on those with unmodifiable factors.

Table 3: Summary of the factors associated with preterm birth

Factors	Unadjusted odds ratio	Adjusted odds ratio
Socio-demographic factors		
Mother's age >35 years	1.47 (1.01, 2.14)	-
Father's age >35 years	1.85 (1.35, 2.55)	-
Never married	2.49 (1.02, 6.09)	-
Low level of maternal education	1.5 (1.08, 2.09)	-
Low level of paternal education	1.57 (1.11, 2.21)	-
Maternal factors & family history		
Obese (>30 kg/m^2 BMI)	2.09 (1.26, 3.48)	-
Having a sister delivered preterm	2.02 (1.23, 3.29)	-
Physical activity		
Daily average >2.5 hours of standing during T1	1.59 (1.17, 2,15)	-
Daily average >2.5 hours of standing during T2	1.49 (1.09, 2.04)	-
Daily average >2.5 hours of standing during T3	1.85 (1.29, 2.65)	1.91 (1.24, 2.94)
Higher level of physical activity during T1	1.45 (1.05, 2.02)	-
Substance abuse		
Betel chewing of spouse	1.49 (1.01, 2.18)	-
Illicit drug use of spouse	8.15 (1.02, 65.51)	-
Environmental factors		
Use of firewood for cooking	1.41 (1.02, 1.93)	1.51 (1.01, 2.25)
High level of dust at home	2.01 (1.27, 3.19)	-
Past & present obstetric & medical factors		
Past history of preterm birth	4.72 (2.25, 9.89)	2.83 (1.09, 7.36)
Previous caesarean section or gynecological surgery	1.69 (1.13, 2.55)	-
Gravidity of 4 or more	3.12 (1.8, 5.31)	2.58 (1.35, 4.9)
Multiple current pregnancy (twin / triplet)	8.36 (2.92, 23.93)	10.57 (3.48, 32.08)
Bleeding or spotting	4.3 (2.39, 7.75)	3.51 (1.77, 6.98)
Pregnancy induced hypertension	3.62 (2.06, 6.37)	2.25 (1.16, 4.38)
Asthma	2.07 (1.19, 3.58)	-
Gestational diabetes (GDM)	1.71 (1.09, 2.67)	-
Psycho-social issues		
Undergone physical assault	3.85 (1.27, 11.63)	-
Stressful life event during pregnancy	2.85 (2.04, 3.98)	-
Stressful life event within last month	4.19 (2.49, 7.04)	2.62 (1.43, 4.81)
Unsatisfied over family support	1.96 (1.26, 3.07)	-
Unsatisfied over own health	3.59 (2.39, 5.37)	2.54 (1.52, 4.22)
Unsatisfied over day-to-day work	2.49 (1.71, 3.63)	-
Unsatisfied over field medical care	2.11 (1.138. 3.92)	-
Unsatisfied over finances	1.83 (1.25, 2.69)	-
Overall unsatisfied	2.92 (1.88, 4.53)	-
Sexual relationship		
Sexual intercourse during pregnancy	0.64 (0.47, 0,88)	-

More than seven days since last sexual intercourse	0.63 (0.4, 0.99)	0.46 (0.26, 0.81)
Oral hygiene		
Unsatisfactory oral hygiene	1.68 (1.19, 2.38)	2.01 (1.33, 3.04)
No dental assessment done	2.64 (1.7, 4.1)	2.16 (1.23, 3.81)

T1, T2 and T3=1st, 2nd and 3rd trimesters

Public Health Implications

- Identifying risk factors that lead to preterm delivery during the antenatal period would lead to reduction of incidence and morbidities attached to it.
- If the risk factors are well known by the first contact health workers, especially public health midwives, precautionary actions could be taken, and the mothers advised based on the risk factor that they possess. Mothers who are at risk can be referred to a hospital where there is a specialized care unit caring for premature babies.

Author Declarations

Competing interests: Authors state no conflict of interest.
Ethics approval and consent to participate: Ethical clearance (RP/ 2017/02 of 20.04.2017) was granted by the Ethics Review Committee of the Faculty of Medicine, General Sir John Kotelawala Defence University Ratmalana, Sri Lanka. Institutional level ethical clearance was also obtained from Colombo south Teaching Hospital and Castle Street Hospital for Women. Administrative clearance obtained from Ministry of Health, Directors of the hospitals and consultants in charge of the obstetric and neonatal units. Informed written consent was obtained from all mothers included in this study.
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Author contributions: DP designed the study, coordinated data collection, and performed the statistical analysis, interpreted the data and drafted the manuscript. RS and KJ contributed to the study by providing their input in the study design, reviewing the statistical analysis and manuscript, and adding technical insights. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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