ORIGINAL ARTICLE

Risk Factors Associated with Low Birth Weight Infants in the Malaysian Population

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SUMMARY

This study aimed to identify the risk factors which were significantly associated with low birth weight (LBW, <2500 g) infants among the Malaysian population. This was a case-control study carried out at the Tuanku Jaafar Hospital, Seremban, Malaysia over a five-month period. Cases were all infants born with birth weight less than 2500g. Control infant were selected with the help a random sampling table from among infants with birth weight of ≥2500g born on the same day in the hospital. Of 3341 livebirths delivered in the hospital, 422 (12.6%) were LBW infants. Logistic regression analysis showed that, after controlling for various potential confounders, the only significant risk factors associated with infants of LBW were gestational age (adjusted odds ratio (OR)=0.6, 95% C.I.: 0.5, 0.6; <0.0001), maternal pre-pregnancy weight (adjusted OR = 0.97, 95% C.I.: 0.95, 0.99; p<0.0001), nulliparity (adjusted OR=3.4, 95% C.I.: 2.2, 5.1; p<0.0001), previous history of LBW infants (adjusted OR=2.3, 95% C.I.: 1.4, 3.8; p=0.001) and PIH during current pregnancy (adjusted OR=3.3, 95% C.I.: 1.6, 6.6; p=0.001). A number of potentially preventable or treatable risk factors were identified to be associated with LBW infants in Malaysia.

KEY WORDS:
Low birthweight, Risk factors, Malaysia

INTRODUCTION

In recent years, low birth weight (LBW, <2500g) has been identified as an important risk factor associated with the subsequent development of various illnesses of childhood and later adult life[1]. When combined with prematurity, LBW has become the second leading cause of death for all U.S. infants, and the leading cause of death for African- American infants[2-5]. Many studies had been done trying to identify the causes of LBW, but the aetiology remains largely unknown[6].

One of the risk factors identified to be significantly associated with LBW infants in the American population is shorter inter-pregnancy interval with resultant maternal nutritional depletion, damage to the reproductive system, and postpartum stress[7]. Many studies have since been conducted to evaluate whether birth spacing is associated with more adverse outcome of the infant, and some reported that the most suitable birth interval is between 18 and 23 month [8-12] and that shorter inter-pregnancy interval is associated with low birth weight babies[6].

In Malaysia, only two studies on LBW infants had been reported previously. The first one reported on the incidence of LBW infant (13.5% among live births at the Maternity Hospital Kuala Lumpur), and that the LBW infants contributed to 74.8% of all infant deaths, with the highest death rate being among Indians, followed by Malays, and Chinese, respectively[13]. A second study reported the incidence of LBW to be 11.84% among live births at the Lundu Hospital in Sarawak, with the lowest incidence being, in descending order, among the Chinese, the Malay, Bidayu, and Iban[14]. However, no study has yet been reported on any risk factors associated with LBW in this country. In view of the findings in America, [8-12] the objective of this study was to identify the risk factors which were significantly associated with LBW infants among the Malaysian population.

MATERIALS AND METHODS

This was a case-control study carried out at the Hospital Tuanku Jaafar, Seremban, Malaysia. All live births delivered at this Hospital over a five-month period, between 15 March 2006 and 14 August 2006, were eligible for the study.

The cases were all infants born with birth weight less than 2500g[15]. For each case of LBW infant identified, one control infant was selected randomly, using a random sampling number table suggested by Hill *et al,* [16] from all infants with birth weight of ≥2500 g born on the same day in the hospital.

The data of each recruited infant were entered into a standardized data sheet after written consent was obtained form the mother. The data information was gathered from the maternal health records and interviewing the mothers of these infants. The data sheet included the following information: [2, 3, 17-20] inter-pregnancy interval, infant's birth weight, gestational age, gender, and maternal basic data, and pre-pregnancy and pregnancy information (including medical problems, ethnic group, education, marital status, age, height and weight, prenatal care utilization, prenatal cigarette smoking, prenatal alcohol consumption, outcome of previous pregnancy, number of previous live births, and medical illness and illness during pregnancy).

Inter-pregnancy interval was defined as the period between delivery and conception, and was computed as the interval between two consecutive deliveries minus the gestational age of the second infant. The interval was calculated in weeks and converted to months (13 weeks was assumed to be equal

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to 3 months)[21, 22]. Infant's gestational age was calculated as the period between the date of the mother's last menstrual period and infant's date of delivery, as recommended by US National Center for Health Statistics[22]. In infants whose mothers were unsure of date, the gestational age assessment of the infants was based on the Ballard score[23].

Maternal education level was recorded in number of formal schooling years attended by these mothers at the date of delivery. Mother's marital status was categorized as married, single and not married, divorced, or widowhood. The number of prenatal visits reported by mothers was used as an indication of their utilization of prenatal care.

Maternal age was defined as number of completed years at time of delivery. Maternal pre-pregnancy height (in cm) and weight (in kg) were based on that recorded in the first maternal antenatal record during the first trimester or recalled by the mothers with late antennal booking. Gravid was defined as the number of all previous pregnancies; while para was defined as the number of previous births, including stillbirths. Previous pregnancies and their outcomes were recorded including number of previous live born infants who had died, number of previous live born infant who were still alive, number of previous spontaneous or induced abortion and also number of previous live born LBW infants. Mother's medical illness was evaluated which included diabetes mellitus, hypertension, asthma, heart disease, and tuberculosis. Illness developed during pregnancy was also recorded; these include gestational diabetes mellitus, pregnancy-induced hypertension (PIH), eclampsia / pre-eclampsia, Rhesus problem, infections and others. All medical conditions were diagnosed based on criteria from Williams Obstetrics[24].

During the study period, the number of all live births delivered each day was recorded to enable calculation of the incidence rate of LBW infants delivered at the Seremban Hospital.

Sample size calculation

Assuming the proportion of infants with normal birth weight with exposure to inter-pregnancy intervals of <18 months or >23 months to be 15%, a sample size of at least 240 in each group was needed to detect an odds ratio of 2.00 at 95% level of confidence with a power of 90% (two tails) [25] in infants with low birth weight.

Statistical analysis

The statistical package SPSS version 11.1 was used for data analysis. Potential risk factors between cases and controls were compared. The unpaired Student t test was used for comparison of continuous variables with normal distribution. The Mann Whitney U test was used for comparison of continuous variables with skewed distribution. The Chi square test (or Fisher Exact test for expected value of less than 5) was used for comparison of categorical variables. Based on the results of univariate analysis a number of potential risk factors associated with LBW infants with p values less than 0.1 were included in a forward logistic regression analysis; these were gestational age, maternal age, maternal pre-pregnancy body weight, ethnic groups, gravida status, parity status, previous history of LBW infants, presence of pregnancy-induced hypertension during current pregnancy, presence of eclampsia during current pregnancy, and paternal smoking habits. Variables were retained in the model if they were significant at p values of less than 0.05 and were not collinear with other variables.

RESULTS

During the study period, there were 3341 livebirths delivered in the hospital. A total of 422 (12.6%) were LBW infants, and 350 of them were recruited as cases. The remaining 72 LBW infants were not recruited because they were discharged home very quickly with their mothers before the investigators could conduct an interview. The following compares the data between the 350 cases and 350 controls recruited.

The LBW infants had significantly lower birthweight ($p<0.0001$) and gestational age ($p<0.0001$) than the controls (Table I). There was no significant difference in their gender or ethnic distribution. Compared with the control infants, a significantly higher proportion of cases were not born by spontaneous vertex delivery (SVD) ($p<0.0001$) and a significantly higher proportion of them had medical problems after birth. There was no significant difference in the maternal age and duration of education between cases and controls. However, the mothers of LBW infants had significantly lower pre-pregnancy weight than the controls ($p<0.0001$).

There was no significant difference in the ethnic distribution, maternal age, maternal educational levels, marital status, past history of abortion, previous history of neonatal deaths, and inter-pregnancy intervals between cases and controls ($p>0.05$) (Table II). There was a significantly higher proportion of primigravida and nulliparous mothers among the LBW group than the controls ($p<0.0001$). There were also a significantly higher proportion of mothers with history of delivering LBW infants previously among the cases than controls ($p=0.002$).

There was no significant difference in the proportions of mothers with medical illnesses, gestational diabetes, rhesus iso-immunisation, VDRL positive, infection, smoking habit and alcohol consumption habits between cases and controls (Table III). However, a significantly higher proportion of mothers of LBW infants had PIH and eclampsia during the current pregnancy than controls ($p<0.001$). Furthermore, a significantly higher proportion of fathers of LBW infants were smokers than controls ($p=0.01$).

Logistic regression analysis showed that, after controlling for various potential confounders, the only significant risk factors associated with LBW in the Malaysian infants were gestational age (adjusted odds ratio (OR)=0.6, 95% C.I.: 0.5, 0.6; <0.0001), maternal pre-pregnancy weight (adjusted OR = 0.97, 95% C.I.: 0.95, 0.99; $p<0.0001$), nulliparity (adjusted OR=3.4, 95% C.I.: 2.2, 5.1; $p<0.0001$), previous history of LBW infants (adjusted OR=2.3, 95% C.I.: 1.4, 3.8; $p=0.001$) and PIH during current pregnancy (adjusted OR=3.3, 95% C.I.: 1.6, 6.6; $p=0.001$). The Nagelkerke R square of the model was 0.44. Maternal age, ethnic groups, gravid status, maternal eclampsia during current pregnancy and paternal smoking habits were not significant risk factors ($p>0.05$).

Table I: Comparison of basic variables of infants and their mothers between low birthweight (LBW, <2500g) infants and controls

Basic variables	LBW infants N=350	Controls N=350	P values
Infants			
Birth weight, g			
Median (IQR)	2200 (435)	3080 (490)	<0.0001*
Gestation, weeks			
Median (IQR)	37 (3)	39 (2)	<0.0001*
Males (%)	173 (49.4)	174 (49.7)	0.6
Modes of delivery (%)			
SVD	192 (54.9)	222 (63.4)	
LSCS	156 (44.6)	124 (35.4)	0.02*
Others	2 (0.6)	4 (1.2)	
Infants with medical problems after birth (%)	152 (43.4)	15 (4.3)	<0.0001*
Mothers			
Mean age, years (SD)	27.8 (6.1)	28.6 (5.4)	0.08
Years of education			
Median (IQR)	11 (2)	11 (2)	0.8
Height, cm			
Mean (SD)	154.1 (6.6)	154.9 (6.5)	0.1
Pre-pregnancy weight, kg			
Median (IQR)	50.0 (15.0)	55.0 (16.0)	<0.0001*

Note: SVD= spontaneous vertex delivery, LSCS= lower segment Caesarean section, SD= standard deviation, IQR= inter-quartile range, * denotes statistical significance.

Table II: Comparison of maternal basic data and their antenatal problems between low birthweight (LBW, <2500g) infants and controls

Maternal variables	LBW infants N=350	Controls N=350	P values
Ethnic groups (%)			
Malay	218 (62.3)	225 (64.3)	0.09
Chinese	35 (10)	49 (14)	
Indian	74 (21.1)	64 (18.3)	
Others	23 (6.6)	12 (3.4)	
Unmarried mothers (%)	4 (1.1)	1 (0.3)	0.2
Gravida			
1	137 (39.1)	79 (22.6)	
2-5	181 (51.7)	238 (68.0)	<0.0001*
6-11	32 (9.1)	33 (9.4)	
Parity			
0	151 (43.1)	84 (24.0)	
≥1	199 (56.9)	266 (76.0)	<0.0001*
No. of abortion (%)			
0	275 (78.6)	291 (83.1)	
1-5	75 (21.4)	59 (16.9)	0.1
No. of neonatal deaths previously (%)			
0	337 (96.3)	340 (97.1)	
1-3	13 (3.7)	10 (2.9)	0.5
No. of LBW infants delivered previously, (%)			
0	276 (78.9)	306 (87.4)	
1-4	74 (21.1)	44 (12.6)	0.002*
Inter-pregnancy intervals among multi-gravid mothers, months			
Median (IQR)	24.0 (39.8)	22.0 (30.0)	0.7

Note: IQR= inter-quartile range, * denotes statistical significance.

Table III: Comparison of maternal illnesses and some parental habits between low birth weight (LBW, <2500g) infants and controls

Parental variables	LBW infants N=350	Controls N=350	P values
Maternal Medical illness			
Hypertension (%)	5 (1.4)	4 (1.1)	0.8
Bronchial asthma (%)	10 (2.9)	18 (5.1)	0.1
Heart diseases (%)	3 (0.9)	3 (0.9)	1.0
Tuberculosis (%)	0 (0)	1 (0.3)	1.0
Maternal illness during pregnancy			
Median lowest Hb level (IQR)	10.7 (1.7)	10.5 (1.4)	0.2
Gestational diabetes (%)	20 (5.7)	20 (5.7)	0.2
PIH (%)	50 (14.3)	17 (4.9)	<0.0001*
Eclampsia (%)	21 (6.0)	4 (1.1)	0.001*
Rhesus iso-immunisation (%)	2 (0.6)	4 (1.1)	0.2
VDRL test positive (%)	0 (0)	1 (0.3)	0.1
Infections (%)	7 (2.0)	6 (1.7)	0.2
Maternal smokers (%)	3 (0.9)	1 (0.3)	0.6
Mothers consumed alcohol during current pregnancy (%)	0 (0)	0 (0)	-
Paternal smokers (%)	220 (62.9)	188 (53.7)	0.01*

Note: Hb= hemoglobin, IQR= inter-quartile range, PIH= pregnancy induced hypertension, VDRL= venereal disease research laboratory,
* denotes statistical significance.

DISCUSSION

A case-control study design was chosen for this study instead of a cross-sectional one because we wanted to a) recruit a sufficient number of LBW infants for the study, and b) study the potential risk factors in greater detail by interviewing the mothers. If it were a cross-sectional study, we would need to recruit a larger number of infants and mothers before the minimal number of LBW infants was recruited. This would mean a larger number of interviewers, which this project did not have the budget to support.

The findings of the present study confirmed that LBW was a common problem in Malaysia,[26] and lower gestational age (i.e. prematurity) was a significant risk factor,[12] after controlling for various potential confounders. Similar to a large population study of 10,240 infants done in Austria,[27] lower pre-pregnancy weight of Malaysian mother was a significant risk factor associated with LBW infants. Unlike the findings of Shiono *et al* [27] which showed no significant difference in the birth weight of infants born to nulliparous women and those with previous childbirths, the present study found that nulliparity was the third most significant risk factor associated with LBW infants among Malaysian. However, similar to the study of Shiono *et al,*[28] we found that a previous history of delivering LBW infants was a significant risk factor. After controlling for potential confounders, we did not find primigravida as a significant risk factor associated with LBW as reported by other investigators[29,30].

Although univariate analysis showed that both maternal PIH and eclampsia were significantly more common among the LBW infants than controls, multivariate analysis showed that only PIH was significantly associated with LBW infants.

Contrary to the findings of a number of investigators,[31-33] maternal ethnicity, marital status, education levels and maternal height were not significant risk factors associated with Malaysian LBW infants. One possible explanation could be the practice of marriage was relatively higher among Malaysian women (>95%) as our culture does not condone unmarried status, and education was quite easily accessible to the population.

Unlike the large population studies reported by Zhu *et al,*[9,10] inter-pregnancy interval was not found to be a significant risk factor associated with LBW in the present study. One possible explanation could be due to the small sample size of our study, which was underpowered to detect any significant difference unlike the 173,205 infants [9] and 435,327 [10] infants recruited by Zhu *et al* in their studies. Similarly, we did not find maternal smoking and alcohol consumption to be significant risk factors among Malaysian LBW infants as these habits were not common among the Malaysian mothers.

Although univariate analysis showed that a history of smoking by the fathers during the current pregnancy was significantly more common among LBW infants, multivariate analysis showed that this was not a significant risk factor associated with LBW infants. One possible explanation for this could be the relatively small sample size of the present study was underpowered to detect any significant difference.

The following are some of the limitations identified in this study. Other than paternal smoking history, history of paternal illness and maternal occupation and drug ingestion, which might have an effect on the birthweight of infants, were not studied. The influence of the 72 LBW infants, who constituted 17% of the eligible LBW infants and were not recruited due to early discharge, could not be ascertained. Nevertheless, based on the findings of the present study, a number of preventable and/or treatable conditions significantly associated with Malaysian LBW infants born in the Hospital Tuanku Jaafar of Seremban have been identified. There is a need for a national study of sufficient sample size to be carried out in Malaysia in the near future, based on an improved study design, to confirm these findings before steps are taken to address or minimize some of all of these risk factors associated with LBW infants in Malaysia.

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