

Risk factors for preterm birth in healthy women of Brunei Darussalam: a retrospective case-control study

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ABSTRACT

Introduction: There has been an increase in the number of preterm births globally in recent years. The major consequences of preterm birth are neonatal mortality and morbidity. This study aims to identify maternal risk factors of preterm birth among healthy pregnant women of Brunei Darussalam.

Materials and Methods: This was a retrospective case-control study involving a total of 260 singleton pregnancies (130 cases and 130 controls) delivered at the Raja Isteri Pengiran Anak Saleha Hospital, a tertiary referral centre in Brunei Darussalam. They consisted of age matched healthy pregnant and control women with no history of medical illness before or during pregnancy. The following information was then obtained from patient medical records: Body Mass Index (BMI), parity, history of preterm birth, ethnicity, secondary smoking exposure, employment status of both mother and father. **Results:** The study population consisted of obese and none obese singleton mothers with an average age of 23 years and were mainly of Malay ethnicity. The following risk factors for preterm birth were identified: parity of five and above ($p = 0.035$) and previous history of preterm birth ($p = 0.030$). Interestingly there was no significant association between preterm birth and previously reported modifiable risk factors such as obesity ($p = 0.396$), ethnicity ($p = 1.000$), employment status of mother ($p = 0.435$), employment status of father ($p = 0.868$) and secondary exposure to smoking ($p = 0.636$). **Conclusion:** The risk factors identified in this study for preterm birth in healthy pregnant women in Brunei Darussalam are parity of five and above and a history of preterm birth. Further studies involving larger sample sizes are needed to confirm the present findings.

Keywords: Preterm birth, risk factors, healthy women, Brunei Darussalam

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INTRODUCTION

Premature or preterm birth is defined as delivery that occurs before 37 weeks of gestation or less than 259 gestational days. ¹ Fifteen million babies (10% of total number of

children born annually) are born preterm and this has increased in recent years² with preterm birth leading to the death of over three million of them.³ The incidence of preterm birth varies with countries, for example, Australia, Canada and Europe having a range of six to eight per cent^{4, 5} and the range for the countries of Africa, Asia and the United States of America (USA) is between nine and 12%.¹ Although the rate of preterm birth in Africa, Asia and the USA are within the same range, developing countries, especially those in Africa and Southern Asia, incur the highest burden in terms of absolute numbers.¹

The major consequences of preterm birth are neonatal mortality and morbidity as well as childhood disability.⁶ Those born preterm have an increased risk of neurodevelopment problems, infections, sensory deficits and respiratory illnesses; the neurodevelopment problems include learning disabilities, mental retardation, cerebral palsy and autism.¹ Preterm birth accounts for approximately 28% of deaths that are not related to congenital abnormality in the first seven days of life worldwide.³ This figure keeps rising and it is indeed the leading cause of perinatal morbidity and mortality in developed countries.^{7, 8}

According to the statistics of health indicators published by the Ministry of Health Brunei Darussalam, there has been an increase in neonatal mortality rate between 2005 and 2009. For example, in the year of 2005 the neonatal mortality rate was 4.5 per 1000 live births (Lbs.) which by 2009 had increased to 5.3 per 1000 Lbs.⁹ Thus, preventing preterm birth may reduce both neonatal mortality and morbidity. Furthermore, it

is of interest that the neonatal mortality rate for Brunei Darussalam a country in Asia is much lower than the Asian preterm birth rate of 10.6%.⁴ However, there is no published data on the incidence of preterm birth in Brunei Darussalam.

Several aetiological risk factors which can be divided into obstetric and non-obstetric risk factors have been identified with respect to preterm birth.^{5, 10} This study focuses on the latter. Previous studies have identified the following non-obstetric risk factors for preterm birth: extremely young and old maternal age^{7, 11}, maternal obesity^{8, 12}, history of premature birth^{6, 10}, parity of above five⁶, multiple births¹³ and cigarette smoking before or during pregnancy.¹³ Although these risk factors have been identified the increase in preterm birth worldwide over the years especially in recent times suggests that there may yet be unidentified risk factors. In addition there is a need to investigate preterm birth in Brunei Darussalam which is important for the country's health planning and local obstetrics care.

The main focus of this study was therefore to investigate the possible relationship between preterm birth in Brunei Darussalam and ethnicity, obesity, parity, history of premature birth and secondary smoking exposure. These factors were chosen because they had variously been reported in the literature to be associated with preterm birth within several different sample populations. This study also examined the correlation between preterm birth and employment status of both mother and father, as this could reveal the impact that socioeconomic status may have on preterm birth.

MATERIALS AND METHODS

This retrospective case-control study was carried out at the Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital, which is the premier tertiary hospital in Bandar Seri Begawan, capital of Brunei Darussalam.

The population used for this study consisted of healthy pregnant singleton women who delivered at the RIPAS Hospital from the 1st January 2010 to 31st December 2010. During the period between 10th December 2011 to 15th March 2012 patient medical records of 130 cases and 130 controls were collected for this study. Cases were defined as women who delivered preterm at a gestational age between 24 weeks + 1 day and 36 + 6 days. Controls were defined as women who delivered term at a gestational age of 37 weeks or more. The cases and controls were matched for age because age is an identified risk factor for preterm birth. Matching for age allows the control of confounding factors in the analysis stage.

Since this study was investigating the non-obstetric risk factors for preterm birth women with self-reported and/or diagnosed medical conditions such as hypertension, anaemia, thyroid disease, diabetes, heart diseases, liver disease, cancer and HIV were excluded from the study. Similarly, women who had complications such as gestational diabetes, preeclampsia and other obstetric factors for preterm birth were also excluded.

The following pieces of information were obtained from patient medical records: Body Mass Index (BMI), parity, history of preterm birth, ethnicity, secondary smoking exposure, employment status of mother and

employment status of father. Parity is defined as the number of times a woman has given birth to a live child. The BMI was calculated by obtaining the weight of the mother (at booking which was during the first encounter of the mother with health professionals during the pregnancy) and dividing it with her height squared which is measured in centimetres.¹⁴ Parity was divided into: nulliparous to four and five or more because a previous study⁶ identified a parity of five and above as a risk factor for preterm birth; furthermore an average family in Brunei has four children¹⁶ even though this may not have a direct impact on preterm birth. At booking time the mother was between 13-18 weeks of gestation. A BMI that equals or is greater than 25 was considered overweight and above 30 as obese.¹⁴ Data for secondary smoking exposure was also obtained from the patient medical records as pregnant mothers were asked whether the husband or anyone in the household they live in smoke.

All data was kept confidential as data is presented in groups so that the identities of individual participants in the study remained anonymous. Approval was obtained from the Medical and Health Research and Ethics Committee of the Ministry of Health Brunei Darussalam prior to the commencement of the study.

Data entry was done and analysis was carried out using the Statistical Package for the Social Sciences (SPSS software) version 18.0 (SPSS Inc 2009). A McNemar's test was used to determine level of significance (p-values) in the association between preterm birth and the factors being investigated in women with preterm birth and control sub-

Table 1: Comparisons between the modifiable risk factors associated with preterm birth (n=260).

Variables	Controls n (%)	Cases n (%)	<i>p</i>
Obesity			
Not overweight or obese	87 (66.9)	79 (60.8)	0.396
Overweight or obese	43 (33.1)	51 (39.2)	
Secondary Exposure to Smoking			
Yes	21 (16.2)	25 (19.2)	0.636
No	109 (83.8)	105 (80.8)	
Occupation of mother			
Home-maker	61 (46.9)	54 (41.5)	0.435
Working	69 (53.1)	76 (58.5)	
Employment status of father			
Employed	109 (83.8)	111 (85.4)	0.868
Unemployed	21 (16.2)	19 (14.6)	

jects. A 'p value' of less than 0.05 ($p < 0.05$) was regarded as significant.

RESULTS

A total of 130 cases and 130 controls were included in the study. Table 1 shows the number of cases and controls within each variable.

A significant association howbeit a relatively weak one was observed between parity of five and above and preterm birth ($p = 0.035$). The number of cases in parity of five and above is 8.4% higher than the number of controls. Women with parity of five and above were more likely to have preterm birth compared to women with a parity of zero to four.

The association between preterm birth and previous history of preterm birth also showed a significant association ($p = 0.030$). The number of cases who had a pre-

vious history of preterm birth was greater than that of the controls.

Comparisons between the cases and controls showed that there was no significant association between preterm birth and obesity ($p = 0.396$), ethnicity ($p = 1.000$), occupation of mother ($p = 0.435$), occupation of father ($p = 0.868$) and secondary exposure to smoking ($p = 0.636$) (Tables 1 and 2).

DISCUSSION

Preterm birth is one of the commonest obstetric problems⁶ and, infants born preterm are more likely to die than infants born full-term due to the complications that can occur in preterm infants such as increased risks of developing respiratory infections in addition to possible underlying congenital defects.⁵ Since preterm birth is a contributing factor to infant mortality it is imperative to always strive to reduce preterm birth rate.

This study did not find any significant association between preterm birth and women who were overweight or obese. This is at variance with the finding from some other studies which have reported a significant association between preterm birth and maternal pre-pregnancy BMI.^{8, 9, 11, 12} In this study, the BMI was calculated from data obtained at booking which was between 13 to 18 weeks into the pregnancy. It is therefore possible that this could be partly responsible for the observed discrepancy even though they may not have gained much weight during this period to affect the BMI calculated.¹³ In addition, differences in the methods of data collection and experimental designs between this study and those of the others may have also played a part in the lack of agreement in the observed data. For example, while this is a retrospective case control study,¹² is a meta-analysis of previously published data. Furthermore, it could be argued that since most of the previous studies were carried out in the developed countries and therefore with a different study population from that of the exclusively Asian population in this study, that The Asia Pacific BMI classification be applied.

On the contrary, we are of the opinion that current WHO BMI is more appropriate for application even in this study. This is in agreement with the recommendation of the WHO Expert Consultation following their observation of a high proportion of Asian people with a high risk of Type 2 diabetes and cardiovascular disease at a BMI lower than the existing WHO cut-off point for overweight.^{14, 15} However, given that: pre-pregnancy obesity leads to an increased risk of preterm birth^{11, 12} and poses a higher risk of developing diseases such as Type 2 diabetes and cardiovascular diseases¹⁵ that may predispose a woman to premature birth because they are more likely to develop complications such as gestational diabetes and preeclampsia, further studies are needed to address this issue.

In this study parity of 5 and above and a history of preterm birth were found to be significantly associated with preterm birth. These two variables had been identified as risk factors for preterm birth.^{6, 8, 13, 17} This is also consistent with studies in the Southeast Asian region such as in Singapore in which they have also found that women with parity

Table 2: Comparison of the non-modifiable risk factors associated with preterm birth (n=260).

Variables	Controls n (%)	Cases n (%)	P-Value
Parity			
Nulliparous to 4	123 (94.6)	112 (86.2)	0.035
5 and above	7 (5.4)	18 (13.8)	
Previous history of preterm birth			
Primigravida or No:	101 (77.7)	83 (63.8)	0.03
Yes	29 (22.3)	47 (36.2)	
Ethnicity			
Malay	121 (93.1)	122 (93.8)	1
Other	9 (6.9)	8 (6.2)	

of 2 and below (a cut off point that is much less than the one used in this study) are less likely to have preterm birth compared to those with parity of 3 and above.¹⁸ This is not surprising as it has been suggested that multiparity may precipitate physiological states capable of causing placental abruption and placental praevia with consequent increase in the likelihood of preterm birth.¹⁹ Therefore, parity of 5 and above and a previous history of preterm birth are risk factors for preterm birth in Brunei Darussalam.

There was no significant association between preterm birth and Malay ethnicity. This contradicts other studies that reported an association between ethnicity and preterm birth.^{13, 19} In the Singapore study with a population mix similar to Brunei but proportionately different¹⁹ the authors observed that Malay ethnicity was more likely to have an effect on preterm birth due to young age, lack of education and no antenatal care. In comparison with the Singapore population there is a greater majority of Malay population in Brunei Darussalam and accounted for about 90% of the present study subjects. Secondly antenatal care is freely and equally available to every Bruneian unlike in Singapore. Taken together these non ethnicity factors may in part but not exclusively be responsible for the observed difference in this and the Singapore study.

Further on ethnicity and preterm birth, an American study found that African American women and Latin American women were more likely to have preterm birth compared to white Americans.¹³ On the contrary another study found that Caucasian teenagers were more likely to have preterm birth

compared to other races such as African American teenagers and Hispanic teenagers.²⁰ Interestingly a London based study of over 122,000 pregnancies with spontaneous onset of labour suggests shorter normal gestational length in Black and Asian women compared with white European women and that foetal maturation may occur earlier in the non white population.²¹ Given that under the British National Health Service (NHS) access to general health care and antenatal care in particular is non discriminatory, it could be argued that the racial differences that have been reported in preterm births^{13, 19, 20} may derive partly at least from the same mechanism(s) governing the race differential spontaneous onset of labour reported in the London study.²¹ Taken together therefore, while race may be a factor affecting preterm birth, these studies suggest that there are other confounding variables such as age and possibly social and cultural factors that must be considered when evaluating the association between ethnicity and preterm birth. This is because different ethnicities have different cultures that contribute to their lifestyle.

The present study investigated a possible association of preterm birth with whether the pregnant mothers are working or home makers. There was no significant association found between working pregnant mothers and preterm birth. This is in contrast to a previous study which reported that working mothers had a lower risk of preterm birth which the authors ascribed to their level of education and availability of antenatal care.²⁰ A number of reasons could account for the difference in observations. Firstly, the present study was carried out in predominantly Malay population of Brunei Darussalam in contrast

to the mix race populations of the United State of America (USA) for the previous study. Secondly, the educational status of the participants in our study is not known and so could not be compared between the study groups. Furthermore in the present study, there was a higher number of working mothers in the cases compared to controls which could skew the observation either way. In addition, the classification does not necessarily reflect the level of physical activity or otherwise of the study subjects which potentially could impact on preterm birth.

Studies have shown that the socioeconomic status of the mother has an effect on the pregnancy.^{13, 20} They showed that working mothers had a lower risk of preterm birth because of the level of education they have and the availability of antenatal care for working mothers.²⁰ This is because in most countries such as the USA medical care is not exclusively provided by the government. Interestingly, in a country such as Iraq where health care is limited, antenatal care visits correlate risk of preterm birth.⁶ This is not the case in Brunei Darussalam where the government provides all health care for free. However, other studies have shown that by limiting the amount of work done by pregnant women and avoiding fatigue helps to reduce the risk of preterm birth.^{5, 20, 22, 23} In this study there are more homemakers in the control group compared to the cases. It could be presumed that a homemaker would have more time to rest: intriguingly, this may not necessarily be true in every case. Although there was no significant association between preterm birth and whether pregnant mothers are in work or homemaking in the present study, a larger cohort study which would dif-

ferentiate between the type of employment and the number of hours the pregnant mothers spend on working in a larger sample is certainly worth pursuing: it may yield a different and more useful result from that of the present study.

This study also shows no significant association between preterm birth and whether father is in employment. The employment status of the father is taken as a reflection of his socioeconomic status or indeed that of the family. This certainly inadequately represents the family's socioeconomic status. Approximately 85% of the fathers, almost equally distributed between preterm and control groups are in employment. In Brunei Darussalam, most of the study population works in the government sector which could possibly be the reason for not finding an association between father's employment status and preterm birth. Rather than taking the employment status of father as a reflection of the family's socioeconomic status, future studies would preferentially correlate preterm birth with the father's employment type and/or family income.

Smoking before or during pregnancy has been identified as a risk factor for preterm birth in other studies.¹⁴ This study investigated the possible association between secondary smoking exposure and preterm birth taking into account that both subjects and controls were non-smokers and less than 20% of each group reported exposure to secondary smoking. There was no association found between secondary smoking exposure and preterm birth. However, there were a higher number of pregnant mothers exposed to secondary smoking in the cases compared

to the controls and may hint of a possible association. In this study, the assumption is that if the husband or anybody in the household smokes then the mother is at risk of exposure to secondary smoking. This may not be the case; therefore a prospective large cohort study would be beneficial in that it would allow us to ask more questions such as whether the father or other household member smokes around the pregnant mother or not.

Another possible reason for not finding an association between secondary exposure to smoking and preterm birth could be under reporting because of the social stigma that may come with smoking. Brunei Darussalam is a relatively conservative country and the Tobacco Order 2005 and Tobacco Laws 2007 which controls the entry, sales, and use of tobacco in public were implemented in the year of 2008. This could be a reason for a possible under reporting of smoking in this study. However, it could be argued that the government has already taken preventive measures to control the use of tobacco and thereby significantly reducing if not totally preventing secondary exposure to smoking. At the moment, no published data or indeed anecdotal evidence supports such an argument.

A recent report of increasing prevalence in smoking amongst girls and young women in Southeast Asia ²⁴ is another relevant point in this matter. This is of significance for at least two reasons. Firstly, none of the study subjects reported being a smoker which may strengthen the under reporting hypothesis. Secondly this has to be taken into consideration in a future study design as this

may inadvertently or otherwise be contributory to precipitating a preterm delivery.

The limitation of this study is the relatively small sample size and the use of a retrospective matched case-control approach. A main disadvantage of using a matched case-control approach is that it can be difficult and time consuming to achieve matched case controls' pairs and does account for confounding variables; in this case it would be age but other variables may also affect the outcome of the study. Therefore for the future, a large prospective cohort study would be undertaken. It is hoped that this would enable researchers to investigate other variables aside from those stated in this study as the risk factors for preterm birth in Brunei Darussalam: the variables may not only occur during pregnancy but also prior to it.

In conclusion, this study has found that parity of 5 and above and a history of preterm birth are risk factors for preterm birth in Brunei Darussalam. Although these risk factors are not modifiable, women who have them can be identified before or early in pregnancy and given the appropriately needed neonatal care to prevent complications. Further studies are needed to investigate other possible risk factors for preterm birth, which may be modifiable to enable better future antenatal care and allow for preventative measures that could decrease the number of preterm births. This could in turn reduce the neonatal mortality and morbidity rates.

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