Risk factors associated with preterm birth in the Dominican Republic: a case-control study

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ABSTRACT

Objectives This study aimed to identify the risk factors associated with preterm birth, and to determine the prevalence of preterm births in the Dominican Republic.

Design Case-control study.

Settings Seven National Reference Hospitals from different regions of the Dominican Republic.

Participants A probabilistic sampling of both cases and controls was performed with a ratio of 2:92:1, and a power analysis was performed with $\alpha=0.05$, $P_1=0.5$, $P_2=0.6$, and $\beta=0.08$, to yield a distribution of 394 cases and 1150 controls. Estimation of gestational age was based on neonatologist reports.

Primary outcome measures A protocol was created to obtain maternal and obstetric information.

Results The main risk factors were a family history of premature births ($p<0.001$, OR: 14.95, 95% CI 8.50 to 26.29), previous preterm birth ($p=0.005$, OR: 20.00; 95% CI 12.13 to 32.96), advanced maternal age (over 35 years; $p<0.001$, OR: 2.21; 95% CI 1.57 to 3.09), smoking ($p<0.001$, OR: 6.65; 95% CI 3.13 to 13.46), drug consumption ($p=0.004$, OR: 2.43; 95% CI 1.37 to 4.30), premature rupture of membranes ($p<0.001$, OR: 2.5) and reduced attendance at prenatal consultations (95% CI 6 to 7, $Z=-10.294$, $p<0.001$).

Conclusion Maternal age greater than 35 years, previous preterm birth, family history of preterm births and prelabour rupture of membranes were independent risk factors for preterm birth. Adolescence, pregnancy weight gain and prenatal consultations, on the other hand, were protective factors for preterm birth. Although the prevalence of premature births in this study was 25%, this could have been biased.

INTRODUCTION

Preterm birth is considered the most important risk factor for perinatal morbidity and mortality. Although a small decline in preterm births has been identified worldwide from the first to the second decade of this millennium, and preterm survival rates have increased in developed countries, preterm neonates still die because of a lack of adequate new-born care in many underdeveloped countries. Regardless of location, identification of the risk factors associated with preterm births is important. Preterm labour and its consequences have been a long-term challenge within the medical field; thus, the purpose of this study is to identify the relevant risk factors in the hope of reducing these fatal consequences.

In general, preterm births primarily pose an elevated risk because they lead to a disproportionate amount of neonatal deaths. For this reason, prematurity is considered a major hindrance to the attainment of the Millennium Development Goals. If the infant survives an increased risk of neonatal infections, it may still show effects related to neurodevelopmental functioning, an increased risk of cerebral palsy, impaired learning and/or visual disorders and chronic diseases in adulthood. High costs of neonatal intensive care and ongoing healthcare must be assumed. Considering the aforementioned scenario, the identification of risk factors is the most essential step for the development of intervention strategies to reduce the number of preterm deliveries and their consequences.

As previously mentioned, preterm neonates have a higher mortality risk in underdeveloped countries. Consequently, the scope of our investigation must include diverse sociodemographic, substance-exposure, etc.
behavioural and clinical data that could be encountered in this area. For example, an association has been reported between preterm birth and maternal education level and parity. Other factors that have been reported to be associated with prematurity include the geographical origin of the mother, the number of prenatal consultations maternal underweight maternal age and pregnancy weight gain. A history of preterm birth has been considered to be the most significant risk factor for preterm birth. Other behavioural and environmental risk factors identified include obesity, stress-inducing life events and sexual activity.

Several risk factors, on the other hand, are related to the mother’s medical history and present medical conditions, such as a previous second-trimester spontaneous abortion, rupture of the fetal membrane, maternal gonourinary infections, high blood pressure, overt diabetes, pre eclampsia, isolated anaemia, bleeding, placental infection and thrombosis.

The risk profile for preterm delivery is undoubtedly multifactorial. However, reliable data on the burden of preterm deliveries in the Dominican Republic are currently lacking. In 1992, a local study in one public hospital found a prevalence of 6.6% and a relative risk for mortality of 25.32, while a study conducted in one of the most popular maternal public hospitals in Santo Domingo in 2009 reported a prevalence of 14.6%. Although these findings imply that the prevalence of preterm births is rising, there are insufficient data to support that argument, and information on the risk factors related to this prevalence is currently unavailable. Therefore, this study aimed to determine the prevalence of, and risk factors associated with preterm births in seven hospitals in the Dominican Republic.

**METHODS**

This study used a hospitalised case-control design with two-stage sampling. Retrospective evaluation of exposure to different potential risks was performed. For this reason, patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research. Confidentiality was protected, and institutional consent was obtained. The data-collection process was conducted in two stages: the first stage was defined by stratified random sampling with hospital domains and affiliate status, and the second stage was defined with a sample of cases and controls of the first stage. In the second stage, the proportion of cases and controls was adjusted to a ratio of 1:4 to achieve the desired power.

Both cases and controls were chosen randomly to achieve maximum efficiency.

**Patient and public involvement statement**

The study was conducted with a retrospective case-control design; therefore, there was no patient involvement in the study protocol or the development of the research questions/outcome. Trained staff collected information from standardised individual records. None of the patients were asked to advise on the interpretation or writing up of the results. Patients and the public were not involved in the development of the research question or study design. Patients and the public will receive oral and written information about this study; however, they are not directly involved in the recruitment and development of the study.

**Participants**

In the first stage, stratified sampling was performed from a population of seven hospitals with fixation based on a sampling fraction system. The sample size, with a 95% confidence level and a 2% margin of error, was 1544 cases. The strata were defined according to the participating hospital and the condition of affiliation with the social security system.

In the second stage, a non-probabilistic sampling of intentional cases and controls was established, which was added to the previously extracted sample based on the following inclusion criteria: having undergone a delivery in a period not more than 12 months before the recruitment of the sample. Cases without a report of gestational age and those with incomplete data were excluded. The case group was delimited on the basis of the estimated gestational age determined in the neonatologist report according to the methods described by Capurro et al. and Ballard et al. A set of instruments with adequate sensitivity and specificity was selected to measure the variables of interest.

**Instrument and data collection**

A protocol was created to determine obstetric data, family history and birth information. The information gathered by this questionnaire can be divided into two main categories: maternal and fetal variables. The maternal variables included information such as the mother’s age, number of prenatal visits, toxic substance consumption, use of antibiotics and previously existing medical conditions. The fetal variables included information such as gestational age at the time of birth, weight, congenital anomalies, mode of delivery, onset of labour (spontaneous or medically indicated), pregnancy outcome (singleton or multiple), birth weight, baby’s sex, prelabour rupture of membranes and antepartum haemorrhage. Trained staff collected information from standardised individual records. To analyse data quality, the measure of inter-rater reliability used was the kappa statistic for categorical variables and the interclass correlation coefficient for continuous variables. All these coefficients ranged from...
0.8 to 1. Preterm birth was defined as a gestational age of less than 37 completed weeks. Prematurity was further categorised as extreme (less than 28 weeks), severe (28–31 weeks), moderate (32–33 weeks), and late preterm or near term (34–36 weeks).

Statistical analysis
The sample distribution for the second stage was estimated using a compromise power analysis for proportions tests (Fisher’s exact test) based on the total sample size estimated in the first stage from the whole population (1544). For this analysis, we chose \( \alpha = 0.05 \), \( P_1 = 0.5 \), \( P_2 = 0.6 \), and \( \beta = 0.08 \), resulting in a control:case distribution of 2.92:1, which represented 394 cases and 1150 controls (matching a total sample of 1544). When testing the hypothesis for an OR in a case-control study, the null hypothesis can be equivalently stated as either exposure OR=1, or \( p_1 - p_2 = 0 \), where \( p_1 \) and \( p_2 \) are the estimated exposure probabilities for cases and non-cases. Because we included many risk factors for testing, probabilities for case and control exposures were estimated assuming a moderate size effect. For this analysis, Gpower software was used. For the rest of the analyses presented in the Results section, SPSS V.24 was used.

RESULTS
Sociodemographic characteristics
The prevalence of premature births in the present study was 25%. Nevertheless, the prevalence varied from 14.8% in the southern regions to 33.3% in the eastern regions of the country, while the data from the most populated area represented approximately 22%–26% of the records studied.

In total, 18.8% (290) of the mothers were adolescents, while mothers aged 20–34 years and those aged ≥35 years constituted 70.7% (1092) and 10.5% (162), respectively, of the study sample. Approximately 92% of mothers in the term and 83% in the preterm group were aged 20–34 years. Almost 60% (57.6%) of all mothers had reached a high school level of education, and only 13.5% had attained higher education. The most common delivery type was a caesarean delivery, representing 59.31% (914) of all cases, and almost 70% of the preterm births belonged to this category (275). However, according to the records, only 7.19% of the births were classified as induced labour, which is a general presentation of preterm labour. The proportion of delayed preterm births in this study was approximately 75% of all cases (297 out of 394), while almost 20% were classified as very preterm births (77 cases). Only 20 cases were classified as extreme preterm births (5%).

Approximately 20% of mothers aged less than 20 years delivered at term, while 14% had preterm deliveries, and this difference was significant (p=0.007, OR: 0.65, 95% CI 0.47 to 0.89). The proportions of mothers aged ≥35 years were significantly different between the two groups (p<0.001, OR: 2.21, 95% CI 1.57 to 3.09). Family history of preterm births (p<0.001, OR: 14.95, 95% CI 8.50 to 26.29), smoking (p<0.001, OR: 6.65, 95% CI 3.13 to 13.46) and drug use (p=0.004, OR: 2.43, 95% CI 1.37 to 4.30) were found to be significantly related to preterm birth (table 1).

A summary of the clinical variable results is presented in table 2. The cases and controls showed significant differences in the incidence of prelabour rupture of membranes (p<0.001, OR: 2.33, 95% CI 1.92 to 3.33), method of pregnancy termination (p<0.001, OR: 0.55, 95% CI 0.42 to 0.69), type of birth termination (p<0.001, OR: 3.90, 95% CI 2.08 to 7.28), use of medicine during pregnancy (p=0.001, OR: 0.328, 95% CI 0.17 to 0.62), tocolytic therapy (p<0.001, OR: 4.549, 95% CI 3.29 to 6.27), and a record of pre-existing medical conditions (p<0.001, OR: 1.722, 95% CI 1.26 to 2.34).

For maternal variables and pregnancy-related variables, a set of Mann-Whitney U non-parametric tests was applied considering the level of measurement and the form of distribution in these factors. Table 3 shows the results of the statistical tests. The preterm and term groups showed no significant difference in terms of the level of education (p=0.422) or weight (p=0.097). The two groups did not show differences in the number of caesarean deliveries (p=0.129), passed deliveries (p=0.584) or abortion (p=0.151). Mothers from the case and control groups differed in terms of previous gestations (p<0.001) and

| Risk factor                      | Term n=1150 | Preterm n=394 | OR      | 95% CI               | P value |
|---------------------------------|-------------|---------------|---------|----------------------|---------|
| History of preterm births       | 20          | 100           | 20.00   | 12.13 to 32.96       | <0.001  |
| Adolescence                     | 234         | 56            | 0.65    | 0.47 to 0.89         | 0.007   |
| Maternal age ≥35 years          | 96          | 66            | 2.21    | 1.57 to 3.09         | <0.001  |
| Family history of preterm births| 17          | 56            | 14.95   | 8.50 to 26.29        | <0.001  |
| Smoking                         | 11          | 23            | 6.50    | 3.13 to 13.46        | <0.001  |
| Alcohol                         | 26          | 19            | 0.24    | 0.02 to 2.53         | 0.314   |
| Drugs                            | 28          | 22            | 2.43    | 1.37 to 4.30         | 0.004   |

n, sample; p, probability of type I error.

Díaz-Rodríguez A, et al. BMJ Open 2021;11:e045399. doi:10.1136/bmjopen-2020-045399
overall weight gain during pregnancy \( (p < 0.001) \). Finally, the sex of the child from preterm birth was primarily female \( (p = 0.029; \text{OR: } 1.259, 95\% \text{CI } 1 \text{ to } 1.59) \).

After adjusting for confounding factors, the results of the multiple logistic regression analyses are presented in Table 4. The significant risk factors for preterm delivery were previous preterm births \( (p < 0.001, \text{OR: } 3.29, 95\% \text{CI } 2.37 \text{ to } 4.56) \), maternal age of 35 years \( (p = 0.09, \text{OR: } 1.59, 95\% \text{CI } 0.92 \text{ to } 2.71) \), family history of preterm births \( (p < 0.001, \text{OR: } 3.47, 95\% \text{CI } 2.43 \text{ to } 4.96) \), and prelabour rupture of membranes \( (p = 0.008, \text{OR: } 1.75, 95\% \text{CI } 1.16 \text{ to } 2.63) \). Three factors showed protective activity: adolescence \( (p = 0.002, \text{OR: } 0.44, 95\% \text{CI } 0.26 \text{ to } 0.75) \), attendance to prenatal consultations \( (p = 0.002, \text{OR: } 0.89, 95\% \text{CI } 0.85 \text{ to } 0.93) \) and pregnancy weight gain \( (p < 0.001, \text{OR: } 0.90, 95\% \text{CI } 0.88 \text{ to } 0.95) \).

### DISCUSSION

This study did not show any relationship between preterm birth and maternal sociodemographic factors, except maternal age of 35 years and adolescence, although the latter appeared to be marginally protective and disappeared when multivariate analysis was performed. Although approximately 19% of all mothers were aged below 20 years, less than 14% delivered prematurely. The number of women who delivered prematurely in this regard was too small to show a significant association with preterm birth and may have inadvertently resulted in a negative association in our study. One plausible explanation for this finding is that the Dominican Republic has an ongoing national project that focuses on providing assistance to pregnant adolescents. Thus, pregnant adolescents may receive increased care during pregnancy, making adolescence a protective factor in the context of pregnancy. The fact that attendance at prenatal consultations was negatively associated with preterm births reaffirmed this possibility.

Previous preterm delivery was associated with subsequent preterm births in this study, which is similar to the findings of other studies. Previous preterm delivery with a family history of preterm births was the most influential risk factor for the occurrence of preterm delivery in this study, consistent with previous studies.\(^{19-23,31,43}\) Univariate analysis also indicated that women receiving prenatal care were less likely to have preterm birth, which has been found in other studies.\(^{44,45}\) Previous studies\(^ {50,46}\) have

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**Table 2** Distribution of clinical characteristics among cases and controls

| Risk factor                                | Term n=1150 | Preterm n=394 | OR  | 95% CI          | P value |
|--------------------------------------------|-------------|---------------|-----|-----------------|---------|
| Uterine anomalies                          | 2           | 2             | 3.09| 0.433 to 22.00  | 0.254   |
| Prelabour rupture of membranes             | 161         | 115           | 2.533| 1.92 to 3.33    | <0.001  |
| Cervical procedures (cone)                 | 6           | 5             | 2.559| 0.77 to 8.43    | 0.153   |
| Isthmic-cervical incompetence              | 12          | 9             | 2.308| 0.96 to 5.52    | 0.500   |
| Cervical stitch                            | 12          | 9             | 2.314| 0.96 to 5.53    | 0.500   |
| Delivery type (caesarean)                  | 20          | 25            | 3.895| 2.08 to 7.28    | <0.001  |
| Genitourinary infection                    | 803         | 271           | 1.050| 0.82 to 1.34    | 0.704   |
| A record of preexisting medical conditions | 864         | 327           | 1.722| 1.26 to 2.34    | <0.001  |

n, sample; p, probability of type I error.

**Table 3** Distribution of past obstetric and gynecological characteristics among cases and controls

| Risk factors       | Medians | Term n=1150 | Preterm n=394 | U     | P value |
|--------------------|---------|-------------|---------------|-------|---------|
| Schooling          | 4       | 4           | 213, 155.0    | 0.422 |         |
| Caesarean deliveries| 2       | 2           | 100, 317.0    | 0.129 |         |
| Gestation          | 3       | 4           | 275, 812.5    | <0.001|         |
| Deliveries         | 2       | 2           | 108, 656.5    | 0.584 |         |
| Abortions          | 2       | 2           | 82, 007.50    | 0.151 |         |
| Weight (pounds)    | 167.46  | 171.16      | 241, 621.5    | 0.097 |         |
| Overall weight gain| 21.88   | 14.96       | 129, 662.0    | <0.001|         |
| Attendance to prenatal consultations | 6 | 4 | –10.294 | <0.001 |     |

n, sample; p, probability of type I error.
shown that women who do not receive prenatal care are more likely to have preterm labour. However, after logistic regression analysis, preterm delivery was only associated with a history of preterm births, maternal age ≥35 years, a family history of preterm births and prelabour rupture of membranes. The variables that were statistically significant and associated with prematurity in the univariate analysis could be considered as risk factors for screening high-risk women who should receive more attention during pregnancy. However, these factors could be correlated; therefore, some of them did not show significance in the multivariate analysis. This is not surprising since the causes of preterm delivery have been shown to vary across locations. For example, education level was not identified as a risk factor, as in other studies and in contrast with other studies. These differences between the risk factors of preterm birth in our country and those in developed countries could be explained by the biased distributions of these variables and the resultant restricted range of correlations. For example, substance exposure, educational levels and smoking were positively biased in our sample.

Notably, the estimates generated by logistic regression analysis of data in this retrospective study should be interpreted with caution, especially since the number of risk factors was small. Considering the complexity of the factors influencing preterm birth, this study had some limitations. First, the findings of our study may have been limited by the handling of missing data in the source documentation because of the use of abstraction techniques. We could not exclude records with missing data since that would have resulted in a very high rate of attrition. Second, our study did not classify preterm births by subcategories. Preterm birth is typically defined as delivery or birth at a gestational age <37 weeks. It can also be classified into three separate subgroups according to clinical presentation: births occurring after spontaneous premature labour, births related to premature contractions and births occurring after spontaneous rupture of the membranes, in which delivery of a premature infant was performed for the benefit of either the infant or the mother. The factors influencing the different subcategories of preterm births need to be further studied. Nevertheless, because of the retrospective nature of this study, this could not be accomplished. Finally, we relied on neonatologist reports for estimation of gestational age because many of our patients did not know their last menstruation date and did not have reliable first trimester sonography data; this factor may have been another limitation since the estimation method used by paediatricians is essentially subjective. In this regard, we highly recommend continuing research on the identification of risk factors using prospective techniques to develop new prematurity predictors to identify high-risk groups and to implement effective interventions to improve birth outcomes.

In conclusion, this study indicated that maternal age ≥35 years, a family history of preterm births and/or rupture of membranes are independent risk factors for preterm birth. Understanding these factors and their interactions could lead to major improvements in the diagnosis, prevention and treatment of preterm births. Although the prevalence of premature births in the study corresponds to 25%, since national reference hospitals are included and some of them have neonatal intensive care units, this prevalence could be biased. One limitation of this study was that it was not possible to clarify whether data were obtained from rural centres because the records did not register that information.

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