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Research Article

Stress, Violence, Depression, and Low Social Support and Their Association with Preterm Birth in a Brazilian Cohort

Lívia Muzzi Diniz Brito,[1] **Ênio Luis Damaso**,[1] **Heloisa Bettiol**,[2] **Viviane Cunha Cardoso**,[2] **Marco Antonio Barbieri**,[2] **Eduardo Carvalho de Arruda Veiga**,[1] **Silvana Maria Quintana**,[1] **and Ricardo Carvalho Cavalli**[1]

[1]*Department of Gynecology and Obstetrics, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil*
[2]*Department of Pediatrics, Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil*

Correspondence should be addressed to Lívia Muzzi Diniz Brito; liviamuzzi@gmail.com

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Background. Studies have identified a trend towards suboptimal birth outcomes, including preterm birth (PTB), in women who experience psychological adversities (stress, depression, domestic violence, and low social support) during pregnancy. *Objective*. To evaluate the association of stress, depression, domestic violence, and low social support with PTB. *Methods*. This is a retrospective cohort study that used data of women assessed between February 2011 and February 2012. The primary outcome of the study was the occurrence of spontaneous PTB < 37 weeks of gestational age. The pregnant women included were evaluated at two different time points: prenatal (between 22 and 25 weeks) and at birth. Sociodemographic data, obstetric history, perceived stress, depression, violence, and social support were collected with a questionnaire and subsequently evaluated and analyzed. Univariate and multivariate log-binomial regression models were constructed to assess the effects of the variables collected on the presence of spontaneous PTB. The SAS 9.3 program was used for all analyses, assuming statistical significance at $p < 0.05$ and a power of the test of 80%. *Results*. A total of 1,370 women were included in the study. The prevalence of PTB was 9.1%. Log-binomial analysis revealed an association between the following characteristics and PTB: smoking (RR 1.64, 95% CI: 1.10-2.44), severe stress (RR 1.82, 95% CI: 1.21-2.73), three or more stressful life events (RR 1.65, 95% CI: 1.05-2.59), and being probably depressed (RR 1.49, 95% CI: 1.02-2.18). However, these associations did not remain significant after multivariate analysis. *Conclusion*. Evidence on the specific effects of depression, violence, anxiety, and stress on birth outcomes remains unclear and at times conflicting. Our results showed no association of the studied parameters with an increased risk of prematurity.

1. Introduction

Studies have shown that pregnancy can be affected by psychological adversities such as anxiety and depression. These adversities can lead to adverse perinatal outcomes, including preterm birth (PTB) and lower birth weight [1].

PTB is defined as delivery that occurs before 37 weeks of gestation [2, 3]. It is an important cause of death in children below the age of five and the leading cause of early neonatal morbidity and mortality, particularly in developing countries [4, 5]. Additionally, PTB accounts for more than half of all long-term morbidity in children, especially among those born before 34 weeks of gestation [6–8].

Despite the existence of strategies for the prevention of PTB such as cervical cerclage [9, 10] and progesterone administration [11–13], premature birth rates have not declined. This fact might be explained in part by the

multifactorial etiology of PTB and by the inadequate selection of patients at increased risk [14].

The cause of PTB remains unknown in about half of the cases, a fact that renders its prediction, as well as its clinical and pharmacological management, a challenge. PTB appears to be the result of a multifactorial process in which the interaction of numerous factors transforms the uterus from a state of quiescence into one of effective contractions [6]. The precursors of PTB vary according to gestational age and social and environmental factors [15]. The risk of spontaneous delivery before 34 weeks increases with age and decreases with maternal height; furthermore, it is higher among women of African and Asian descent compared to white women, as well as among smokers and women who became pregnant using ovulation-inducing drugs [15]. In addition to risk factors for spontaneous preterm delivery, some psychosocial factors appear to be related to PTB, such as stress, domestic violence, depression, and social support [16, 17]. However, evidence on the specific effects of antenatal depression, anxiety, and stress on birth outcomes remains unclear.

The main objective of this study was to evaluate the association of psychosocial risk factors such as stress, domestic violence, depression, and low family support with the occurrence of PTB in a Brazilian cohort.

2. Methods

2.1. Study Design. This was a prospective cohort study of consecutive singleton pregnancies from Ribeirão Preto, Brazil, between February 2011 and February 2012. The data were obtained from the "Etiological Factors of Preterm Birth and Consequences of Perinatal Factors for Child Health: Brazilian Birth Cohort Study of Ribeirão Preto and São Luís – BRISA" in 2010 [18].

The city of Ribeirão Preto is located in the northeastern region of the State of São Paulo, a rich and industrialized region with a Human Development Index (HDI) of 0.800 in 2010, occupying the 40th position in Brazil [19]. Its population was 604,682 inhabitants in 2010 [20]. Ribeirão Preto is one of the most developed cities in the country, with 99% of all residences receiving piped water and being equipped with a sewage system [20].

2.2. Protocol and Population. The reference population consisted of pregnant women who received prenatal care at public and private health services in Ribeirão Preto, Brazil. The cohort sample size was calculated according to the reported prevalence of the explanatory variables of the project, which ranged from 10 to 50%, and considering a predicted rate of prematurity of 12%. Thus, 1,500 pregnant women were recruited in Ribeirão Preto and invited for interview during the prenatal period. The women were again interviewed after the birth of their babies. On that occasion, the hospitals of the city were monitored daily for the identification of women belonging to the cohort.

The eligibility criteria included a singleton pregnancy with a structurally normal fetus at enrollment and obstetric ultrasound performed at less than 20 weeks of gestation. The exclusion criteria were a failure to collect data from the questionnaires, medical records or through telephone calls, loss to follow-up, miscarriage, intrauterine fetal death, the presence of major congenital anomalies at birth, and iatrogenic preterm delivery.

2.3. Data Collection. Previously trained undergraduate students contacted the women during the prenatal period at ultrasound clinics, prenatal outpatient clinics, and public and private maternity hospitals. Women who underwent obstetric ultrasound before the 20th gestational week, when gestational age is determined more reliably, were invited to participate. The interviews were held at the Clinical Research Unit of the University Hospital, University of São Paulo, in Ribeirão Preto.

At the site of data collection, the subjects gave written informed consent to participate in the study, responded to a general prenatal questionnaire and a self-applied questionnaire, and were submitted to anthropometry (weight, height), blood pressure measurement, collection of biological specimens (blood, urine, and vaginal secretion), and dental and ultrasound examination. Two standardized questionnaires were used for data collection: one was applied by the interviewers, and the other was self-administered.

The pregnant women included were evaluated at two different time points: prenatal (between 22 and 25 weeks) and at birth. Standardized questionnaires were used for data collection at these two time points. Maternal characteristics were collected by analysis of the questionnaires, medical records, and telephone calls to the patients.

2.4. Maternal Variables and Definitions. The primary outcome of the study was the occurrence of spontaneous PTB, which was defined as all deliveries with spontaneous onset of labor or with preterm prelabor rupture of membranes leading to birth before 37 weeks of gestation. The following characteristics were analyzed: sociodemographic variables (age, parity (including pregnancy during data collection), history of PTB, educational level, marital status, and social class (defined according to the Brazilian Association of Research Companies—ABEP in the Portuguese acronym: classes A, B, C, and D/E)) and variables related to pregnancy, prenatal care, and delivery (consumption of alcoholic beverages, illicit drug use and smoking during pregnancy, and gestational age at birth).

The educational level was divided into low (up to incomplete elementary school), intermediate (up to incomplete high school), and high (with complete high school or higher).

The social class (ABEP categories) was defined based on average monthly income: A (>20 minimum wages), B (>10 and ≤20 minimum wages), C (>4 and ≤10 minimum wages), D (>2 and ≤4 minimum wages), and E (≤2 minimum wages) [21]. At the time of the study, the minimum wage in Brazil was US$ 267.81. The classes were regrouped into only three categories based on monthly income: ≤2 minimum wages (E), >2 to ≤10 minimum wages (C and D), and >10 minimum wages (A and B).

Gestational age was calculated from the last menstrual period and confirmed by crown-rump length measurement during the first-trimester ultrasound. In the case of discrepancy of more than seven days between the gestational age provided by last menstrual period and ultrasound, the sonographic gestational age was used.

Perceived stress was evaluated using the Perceived Stress Scale (PSS), which consists of 14 questions scored in order of frequency from 0 to 4. For validation in the Brazilian population, the authors proposed a short version consisting of only 10 items (PSS10) [22]. The total sum of the 10 items results in a score of 0 to 40, for which no division into preestablished scores exists. Most questions reflect negative feelings and the inability to deal with stress, although some questions address positive emotions and the ability to act in stressful situations. All items are designed to identify to what extent the respondents evaluate their life as unpredictable, uncontrollable, and overloaded and include central components of the experience of stress. For analysis, the participants were divided into sample distribution terciles as follows: low score (mild stress), medium score (moderate stress), and high score (severe stress). Stress was considered to be present when >75th percentile.

For data collection of the stressor events in the last 12 months, eight items of the Stress-Producing Life Events (SPLE) instrument were used according to the procedure described by Lopes and Faerstein [23], included in the Self-Applied Prenatal Questionnaire of the BRISA project. The items were assessed using a list with dichotomous responses (yes, no) in order to measure the number of stressors in the last 12 months. The following items were included: a health problem that resulted in the interruption of usual activities for more than one month, hospital admission due to illness or accident, death of a close relative, severe financial difficulties, forced relocation of housing, separation or divorce, physical aggression, and theft or robbery. Despite the existence of severity scales for the assessment of stressful events, studies prioritize the use of direct and simple questions and evaluate the role of the occurrence of more than one event by the score related to the number of events [24].

The Center for Epidemiological Studies-Depression Scale (CES-D) [25], translated and adapted to Portuguese in 1998, was used to assess depression. There are 20 items designed to detect depressive symptoms, with questions related to mood, behavior, and perception. The score is divided into "irrelevant symptoms," "possibly depressed," and "probably depressed".

The questionnaire used to evaluate violence consists of 13 questions obtained from the Portuguese version of the World Health Organization questionnaire translated and validated for Brazil [26] in the "Violência contra Mulher" study. The questionnaire assesses three types of violence: sexual, physical, and psychological. The response options are "no," "once," "a few times," or "many times." An affirmative answer to any of the items was classified as "yes" for the purpose of association analysis. The responses were subsequently divided according to the type of violence experienced.

There are few validated instruments in Brazil to measure social support. The few existing studies used the Social Support Survey of the Medical Outcomes Study (MOS). This scale was translated and adapted to Portuguese after validation and use in the "Pró-Saúde" study, a cohort of employees of a Brazilian public university [27]. The instrument consists of five social support domains: material, affective, positive social interaction, emotional, and information. There are five response options: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, and 5 = constantly. As done for the assessment of perceived stress, the level of social support was divided into terciles in view of the result of the sample, and the pregnant women were classified into three groups: low, medium, and high social support.

2.5. Ethical Considerations. The study was conducted in accordance with the criteria of Resolution 196/96 of the National Health Council, and its complementary norms and all of its phases were approved by the Research Ethics Committee of the University Hospital, FMRP/USP (Protocol No. 4116/2008). Mothers who agreed to participate in the study gave written informed consent and were informed that they could withdraw from the study at any time with no harm to themselves or their families. Consent for underage mothers was also obtained from the parents or guardians.

2.6. Statistical Analysis. The data of each patient were entered into Excel spreadsheets for the creation of a database. First, exploratory analysis of the data was performed. Quantitative variables were reported as the mean and standard deviation and qualitative variables as absolute and relative frequencies.

Binomial logistic multiple regression was performed, and the unadjusted and adjusted relative risk (RR) and 95% confidence interval (95% CI) were calculated. Univariate analysis of the covariates described was used to identify predictors of spontaneous PTB. All variables with $p < 0.05$ in univariate analysis were included in the multivariate model. The SAS 9.3 program (SAS Institute, Inc., Cary, NC, USA) was used for all analyses, assuming statistical significance at $p < 0.05$ and a power of the test of 80%.

Unanswered questions or data not computed in the database were considered missing data and were excluded from the final analysis.

3. Results

A total of 1,400 women were recruited and answered the questionnaires applied during the prenatal period; information was collected at birth from 1,370 of these women. Among the 1,370 pregnant women evaluated, 133 (9.7%) had spontaneous PTB (<259 days).

Table 1 shows the demographic characteristics, obstetric history, and data related to stress, violence, and social support. The results of association analysis between these characteristics and PTB (<37 weeks) by log-binomial regression are also shown.

There was a predominance of women aged 18 to 35 years ($n = 1164$, 85%). Most of the participants had completed elementary school or incompleted high school ($n = 1031$, 75.5%) and lived with a partner ($n = 1106$, 80.9%). An

Table 1: Demographic characteristics, obstetric history, and data related to stress, violence, and social support of the women studied regarding the outcome (presence or absence of preterm birth) and risk factors for preterm birth in univariate analysis.

Variable	Spontaneous preterm birth			95% CI		
	No (n = 1,237) n (%)	Yes (n = 133) n (%)	Total (n = 1,370) n (%)	Unadjusted RR	LL	UL
Age (years)						
<18	99 (8)	9 (6.77)	108 (7.9)	0.87	0.45	1.67
18–35	1,053 (85.13)	111 (83.46)	1164 (85)	Ref	Ref	Ref
>35	85 (6.87)	13 (9.77)	98 (7.1)	1.39	0.81	2.37
Education						
Incomplete elementary school	197 (15.98)	27 (20.30)	224 (16.4)	1.33	0.67	2.66
Complete elementary school	935 (75.83)	96 (72.18)	1031 (75.5)	1.03	0.55	1.92
Complete high school and/or higher	101 (8.19)	10 (7.52)	111 (7.1)	Ref	Ref	Ref
Household income						
<2 MW	343 (30.68)	38 (31.67)	381 (30.8)	0.923	0.349	2.442
2 to 10 MW	742 (66.37)	78 (65.00)	820 (66.2)	0.880	0.341	2.273
>10 MW	33 (2.95)	4 (3.33)	37 (3)	Ref	Ref	Ref
Partner						
No	229 (18.54)	33 (24.81)	262 (19.1)	1.39	0.96	2.01
Yes	1,006 (81.46)	100 (75.19)	1106 (80.9)	Ref	Ref	Ref
Alcohol consumption						
No	927 (75.18)	94 (70.68)	1021 (74.7)	Ref	Ref	Ref
Yes	306 (24.82)	39 (29.32)	345 (25.3)	1.22	0.86	1.74
Smoking						
No	1,083 (87.83)	107 (80.45)	1190 (87.1)	Ref	Ref	Ref
Yes	150 (12.17)	26 (19.55)	176 (12.9)	**1.64**	**1.10**	**2.44**
Illicit drug use						
No	1,174 (95.76)	129 (97.73)	1303 (95.9)	Ref	Ref	Ref
Yes	52 (4.24)	3 (2.27)	55 (4.1)	0.55	0.18	1.67
Parity						
1	617 (49.88)	59 (44.36)	676 (49.3)	Ref	Ref	Ref
2	362 (29.26)	39 (29.32)	401 (29.3)	1.11	0.75	1.63
3 or more	258 (20.86)	35 (26.32)	293 (21.4)	1.36	0.92	2.03
History or preterm birth						
No	1,132 (91.88)	118 (89.39)	1250 (91.6)	Ref	Ref	Ref
Yes	100 (8.12)	14 (10.61)	114 (8.4)	1.30	0.77	2.18
Stress						
Mild	423 (34.2)	33 (24.81)	456 (33.3)	Ref	Ref	Ref
Moderate	419 (33.87)	40 (30.08)	459 (33.5)	1.20	0.77	1.87
Severe	395 (31.93)	60 (45.11)	455 (33.2)	**1.82**	**1.21**	**2.73**
Number of stressful life events						
None	460 (37.19)	41 (30.83)	501(36.5)	Ref	Ref	Ref
1 or 2	598 (48.34)	64 (48.12)	662 (48.3)	1.18	0.81	1.71
3 or more	179 (14.47)	28 (21.05)	207 (15.1)	**1.65**	**1.05**	**2.59**
General violence						
No	678 (54.81)	74 (55.64)	752 (54.9)	Ref	Ref	Ref
Yes	559 (45.19)	59 (44.36)	618 (45.1)	0.97	0.70	1.34
Psychological violence						
No	692 (55.94)	75 (56.39)	767 (56)	Ref	Ref	Ref
Yes	545 (44.06)	58 (43.61)	603 (44)	0.98	0.71	1.36

Table 1: Continued.

Variable	Spontaneous preterm birth				95% CI	
	No (n = 1,237) n (%)	Yes (n = 133) n (%)	Total (n = 1,370) n (%)	Unadjusted RR	LL	UL
Physical violence						
No	1,084 (87.63)	116 (87.22)	1200 (87.6)	Ref	Ref	Ref
Yes	153 (12.37)	17 (12.78)	170 (12.4)	1.03	0.63	1.67
Sexual violence						
No	1,189 (96.12)	129 (96.99)	1318 (96.2)	Ref	Ref	Ref
Yes	48 (3.88)	4 (3.01)	52 (3.8)	0.78	0.30	2.04
Depression						
Irrelevant symptoms	628 (50.77)	56 (42.11)	684 (50)	Ref	Ref	Ref
Possibly depressed	308 (24.9)	35 (26.32)	343 (25)	1.24	0.83	1.86
Probably depressed	301 (24.33)	42 (31.58)	343 (25)	**1.49**	**1.02**	**2.18**
Social support						
Low	411 (33.23)	46 (34.59)	457 (33.4)	Ref	Ref	Ref
Medium	413 (33.39)	43 (32.33)	456 (33.2)	0.93	0.63	1.39
High	413 (33.39)	44 (33.08)	457 (33.4)	0.95	0.64	1.41

MW: minimum wage (US$ 267.81); n: sample number; RR: relative risk; LL: lower limit; UL: upper limit.

important percentage (n = 820, 66.2%) had an average monthly household income of 2 to 10 minimum wages. A minority were alcohol drinkers (n = 345, 25.3%), smokers (n = 176, 12.9%), and illicit drug users (n = 55, 4.1%). Regarding obstetric history, most women were primiparous (n = 676, 49.3%), and only a small percentage had a history of PTB (n = 114, 8.4%).

The evaluation of perceived stress and of the number of stressful events showed that practically one-third of the respondents experienced mild stress and one-third moderate and severe stress; 662 (48.3%) women reported one or two stressful events. Regarding violence, 618 (45.1%) women reported having suffered some type of violence, with psychological violence being the most significant reported by 603 (44%) of the women. With respect to social support, the same percentages of women reported a low, medium, and high level of support.

Log-binomial regression analysis revealed an association between the following characteristics and PTB (<37 weeks): smoking (RR 1.64, 95% CI: 1.10-2.44), severe stress (RR 1.82, 95% CI: 1.21-2.73), three or more stressful life events (RR 1.65, 95% CI: 1.05-2.59), and being probably depressed (RR 1.49, 95% CI: 1.02-2.18).

We then performed multivariate analysis including these factors (smoking, stress, stressful life events, and depression). None of the risk factors was associated with PTB in this second analysis, as shown in Table 2.

4. Discussion

The main findings of this study were a rate of spontaneous PTB of 9.7% and the association of these deliveries with smoking, severe stress, three or more stressful events, and being probably depressed only in the univariate analysis. In multivariate analysis, in which the variables were included as covariates to adjust for confounding, none of these factors remained associated with spontaneous PTB.

A study on the prevalence of PTB in 184 countries estimated the birth of approximately 14.9 million preterm babies in 2010, corresponding to 11.1% of all live births worldwide; this percentage ranged from about 5% in several European countries to 18% in some African countries [28]. In Brazil, there have been advances in maternal and child health care since the 1990s, but the number of PTB is still increasing [29]. The "Nascer no Brasil" study [30] identified a prevalence of PTB of 11.3% in 2011.

Several factors have been associated with PTB, including maternal demographic characteristics, social and economic factors, medical complications, obstetric history, and specific conditions of the current pregnancy [15, 31, 32]. However, PTB risk scores are disappointing owing to both low sensitivity and a poor positive predictive value, especially among nulliparous women because they have no history of PTB [33]. Improvement in the identification of patients at risk of PTB is therefore a prerequisite for reducing the incidence of prematurity. Social and economic disadvantages are persistently associated with an increased risk of PTB. Within this context, lower educational attainment, geographic residence, and lack of access to prenatal care are all linked to significantly higher rates of PTB [34]. Although many of these individual associations are statistically significant, each factor alone does not show a strong association with PTB [35].

Many of the risk factors for PTB are potentially modifiable, including smoking. Tobacco use is associated with an increased risk of PTB, probably through vasoconstrictive and hypoxia-mediated pathways [36]. Furthermore, a history of PTB is a very strong predictor of subsequent PTB [37]. The number of prior preterm deliveries and the degree of prior prematurity significantly affect the risk of recurrent PTB [38].

Table 2: Relative risk for preterm birth in multivariate analysis.

Variable	Adjusted RR	95% CI	
		LL	UL
Smoking			
No	Ref	Ref	Ref
Yes	1.44	0.92	2.24
Stress			
Mild	Ref	Ref	Ref
Moderate	1.14	0.70	1.86
Severe	1.65	0.97	2.81
Number of stressful life events			
None	Ref	Ref	Ref
1 or 2	1.03	0.68	1.54
3 or more	1.25	0.73	2.13
Depression			
Irrelevant symptoms	Ref	Ref	Ref
Possibly depressed	1.03	0.65	1.63
Probably depressed	0.95	0.56	1.59

RR: relative risk; LL: lower limit; UL: upper limit.

We found no association of these variables already established in the literature as risk factors with spontaneous PTB. This divergent result might be explained by the use of a convenience sample in our study, by the sample size, or even by the fact that the risk factors show a stronger association when analyzed together rather than separately.

In our sample, perceived stress and the number of stressful events appeared to increase the risk of PTB in the unadjusted analysis, although this effect was not observed in multivariate analysis. This association has been increasingly demonstrated in the current literature. In a systematic review, Shapiro et al. [39] evaluated 107 articles, and most studies reported positive results, with the RR ranging from 1.2 to 2.1 for the association between higher levels of perceived stress and PTB.

Psychosocial stress includes anxiety caused by several factors (e.g., gender, racial discrimination, food scarcity, and homelessness) across the life course. Stress induces the secretion of cortisol-releasing hormone that leads to increases in prostaglandins and inflammatory cytokines, factors associated with uterine contractions and spontaneous PTB [40]. Despite biological plausibility, studies examining the impact of psychosocial stress on PTB have found inconsistent results [41, 42], possibly due to the poorly characterized interaction between psychosocial stress and other risk factors.

Our data showed that depression tends to increase the risk of PTB, but this risk did not persist in multivariate analysis. Data in the literature are controversial. In a study including 7,267 women in the United States, Venkatesh et al. [43] demonstrated a strong association between positive screening for antenatal depression and PTB, even after adjusting for covariates. Another study involving an even larger sample of 366,499 pregnant women in Sweden [44] confirmed the association between maternal depression and PTB. Unlike the present project, both studies were designed to directly evaluate depressive disorders in larger populations and with easy access to electronic charts and data such as antidepressant use and previous consultations. The fact that we depended exclusively on a self-administered questionnaire with low specificity for screening is a weakness of this study and may be a source of bias.

With respect to domestic violence, our study also found no significant association. On the other hand, a study of 150 pregnant women conducted in India [45], a country with the largest absolute number of maternal deaths in the world and very high rates of domestic violence, showed a 3.9-fold (CI 1.19-12.82) increased risk of PTB associated with psychological violence. In Peru, a study conducted in 2012 on 959 women found a RR of 2.1 (CI 1.59–2.68) for the association with a history of partner violence [46].

Finally, although social support is considered an important mechanism to reduce the negative effects of stress and help the pregnant woman develop mechanisms for coping with stressful events, this "protective effect" has not been demonstrated in the literature. The present results regarding social support are no different. A review of 16 studies found no direct association between social support and PTB; there was only an association when this variable was analyzed together with perceived stress [47].

A strength of this study is the large, nonrandom sample selected from the general population and the application of internationally validated questionnaires used in similar studies. The assessment of violence was confidential, a fact that increases reliability. All patients underwent two interviews on two important occasions, in the second trimester and after delivery, which were held by trained personnel.

The limitations include the lack of application of the violence questionnaire after birth, the lack of patient follow-up from recruitment to birth, and the fact that no serum markers of stress were collected. Unlike studies conducted in developed countries, no universal electronic medical records that contain more consistent information about the personal history of each pregnant woman or the use of antidepressants, hospitalizations, or previous diagnoses are available in Brazil. Only the health information obtained with questionnaires is considered, which may be subject to bias in data collection. Likewise, only birth-related data reported by the patients were used, which are also subject to bias, especially the procedures performed and the cause of PTB. By analyzing information and perceptions reported by the patients, each analysis is prone to a high degree of subjectivity, as is any study that assesses the perceived level of stress, violence, depression, and social support.

It should be noted that the present data were collected in 2011 and 2012 and would therefore need to be revised, especially after the COVID-19 pandemic that had a great social, economic, and psychological impact on the population and certainly changed the results [48].

5. Conclusion

Our results showed no association of depression, stress, violence, or social support with an increased risk of prematurity.

Data Availability

The data and materials that support the findings of this study are available from the corresponding author, Ênio Luis Damaso, upon reasonable request, and they were uploaded in submission.

Conflicts of Interest

The authors have no competing interests as defined by BMC or other interests that might be perceived to influence the results and/or discussion reported in this paper.

Authors' Contributions

LMDB has made substantial contributions to the conception and design of the study and definition of intellectual content and has been involved in literature search, data analysis, statistical analysis, manuscript preparation, manuscript writing, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. ELD, HB, VCC, and MAB have been involved in literature search, data analysis, statistical analysis, and final approval of the version to be published. ECAV has made substantial contributions to the conception and design of the study and definition of intellectual content, manuscript writing, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. SMQ has been involved in literature search, data analysis, statistical analysis, manuscript preparation, manuscript writing, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. RCC has been involved in literature research, manuscript preparation, manuscript writing, and final approval of the version to be published. Lívia Muzzi Diniz Brito, Ênio Luis Damaso, Eduardo Carvalho de Arruda Veiga, Silvana Maria Quintana, and Ricardo Carvalho Cavalli contributed equally to this work. Heloisa Bettiol, Viviane Cunha Cardoso, and Marco Antonio Barbieri contributed equally to this work.

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