




Regular Article

High-risk pregnancy and its relationship with the neurodevelopment and behavior of 2-year-old children

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Abstract

High-risk pregnancies elevate maternal stress, impacting offspring neurodevelopment and behavior. This study, involving 112 participants, aimed to compare perceived stress, neurodevelopment, and behavior in high-risk and low-risk pregnancies. Two groups, high-risk and low-risk, were assessed during pregnancy for stress using hair cortisol and psychological analysis. At 24 months post-birth, their children's neurodevelopment and behavior were evaluated. Results revealed higher perceived stress and pregnancy-related concerns in high-risk pregnancies, contrasting with low-risk pregnancies. Offspring from high-risk pregnancies displayed elevated internalizing behavior scores, while low-risk pregnancies showed higher externalizing behavior scores. Additionally, women in low-risk pregnancies exhibited increased cortisol concentrations 24 months post-delivery. These findings underscore the necessity for early stress detection and prevention programs during pregnancy, particularly in high-risk cases, to enhance maternal and infant health.

Keywords: child development; cortisol; high-risk pregnancy; infant development; psychological stress

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Introduction

Pregnancy is a stage in the life of women that implies physical and psychological changes, which may present complications, leading to high-risk pregnancy. Due to these substantial changes, the health and life of both the mother and the infant are at greater risk (NICHD, 2020), thus it is a condition that requires specialized medical care. According to Holness (2018), there are four types of risk factors: psychosocial factors, medical history, bad obstetric history, and typical conditions of pregnancy.

Some of the causes of high-risk pregnancy are maternal age (over 35 years of age or adolescent), obesity or overweight, psychiatric diseases, autoimmune diseases, pre-eclampsia, gestational diabetes, threatened preterm labor, multiple pregnancy, and maternal infectious disease (Holness, 2018).

The psychological consequences of this type of pregnancy are related to the fact that women with high-risk pregnancy present a greater prevalence of psychological disorders, especially anxiety, depression and stress, compared to women with low-risk

pregnancy (Williamson et al., 2023). This could be due to the greater concerns shown by high-risk pregnancy women about their health and that of their children, as well as the complications that may derive from the labor (Mohammadi et al., 2022; Ray et al., 2022). Another possible explanation is that they tend to experience greater feelings of guilt and difficulty to manage their emotions, as they feel responsible for what may happen to their babies (McCoyd et al., 2020). They also tend to be afraid throughout the pregnancy, and there may appear feelings of frustration, isolation, loneliness, rage, and depression, which are all related to the hospitalizations and the severity of their diagnosis (Isaacs & Andipatin, 2020).

In general, these women experience the period of pregnancy with moments of uncertainty and threat, which generate high levels of stress, potentially affecting their offspring. In this line, the fetal programming hypothesis (Barker, 2007) states that the biological development of the fetus can be affected by the exposure of the mother to adverse environmental situations, such as bad nutrition, stressful events and infections, in sensitive periods of pregnancy, producing excess maternal glucocorticoids, which have a negative impact on placental function (Chen et al., 2019), leading to a greater probability of developing chronic diseases, even in adulthood (Shchurevska, 2022; Van Den Bergh et al., 2020).

Specifically, prenatal stress has different negative effects on the development of the offspring. Different studies have analyzed its influence on the shortening of telomeres, which is associated with

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shorter life (G FC;m FC;§, 2022). Moreover, maternal anxiety has been related to other adverse perinatal results, such as premature birth, low birthweight (Sanjuan et al., 2021), and shorter cephalic perimeter (Grigoriadis et al., 2018). Other studies have associated it with a greater probability of developing behavior disorders in the offspring (Madigan et al., 2018). In this line, Santelices et al. (2021) found that children of mothers who had suffered from depression during pregnancy were more likely to develop externalizing behaviors.

Deficiencies have also been detected in social communication and language, which are related to autism spectrum disorders (Brachetti et al., 2020), anxiety and depression (Davis et al., 2020; Hentges et al., 2019; McLean et al., 2018), motor problems, deficient cognitive development, and alterations in brain development (Van Den Bergh et al., 2020).

These alterations are associated with structural changes in the limbic and frontotemporal networks (cortical thinning and enlarged amygdala) and in the functional and microstructural connections that link them (Lautarescu et al., 2020), and they may be related to an over activation of the hypothalamic-pituitary-adrenal (HPA) axis in cases of stress, which increases the level of glucocorticoids, including cortisol, eventually affecting the fetus (Monk et al., 2019).

The influence of high-risk pregnancy on the neurodevelopment and behavior of the offspring has been poorly studied. For instance, in contrast with what would be expected, Romero-Gonzalez et al. (2020) reported that 6-month-old babies born from high-risk pregnancies presented a better cognitive, language and motor development than babies born from low-risk pregnancies.

Other studies have related different prenatal risk factors to the behavior of the offspring. Marceau et al. (2013) found a relationship between perinatal risk factors and the genetic and environmental influences on child behavior. On the other hand, different authors have analyzed, separately, the influence of different prenatal risk factors on the behavior of the infants (Krzczkowski et al., 2019; Tien et al., 2020). However, these studies do not address, specifically, how the type of pregnancy risk (high or low) influences the behavior of the offspring.

For the above mentioned, and taking into account that high-risk pregnancy entails greater maternal stress levels, which can have a negative effect on the infant, the aim of the present study was to analyze the possible differences in the level of stress between women with high-risk pregnancy and women with low-risk pregnancy, throughout pregnancy and at 24 months after delivery, as well as to explore the possible consequences of high-risk pregnancy on the neurodevelopment and behavior of their offspring at 2 years of age. We hypothesize that women with high-risk pregnancies will have higher levels of stress (psychological and physiological through cortisol) in comparison to those with low-risk pregnancies. In addition, we hypothesize their children will portray higher behavioral issues.

Method

Participants

The sample was constituted by a total of 56 pregnant women ($M = 34.43$ years; $SD = 3.46$) and their 56 children (26 boys and 30 girls), who were evaluated at 24 months of age ($M = 24.08$; $SD = 0.82$). The women were divided according to the type of pregnancy risk, with 27 women in the high-risk group and 29 women in the low-risk group.

The participants were informed about the study in the first pregnancy visit to the obstetrician, in a health center of Granada (Spain), where, after agreeing to participate voluntarily, they read the information sheet and signed the informed consent form.

The inclusion criteria were: (1) being pregnant, (2) being at least 18 years old, (3) mastering the Spanish language, both orally and in written, and (4) in the case of the high-risk pregnancy group, having a medical diagnosis of this condition. The study excluded women who suffered from psychiatric diseases that required treatment and/or the intake of corticoids.

The study was conducted in compliance with the Declaration of Helsinki (World Medical Association, 2013) and the guidelines of Good Clinical Practice (Directive 2005/28/CE) of the European Union. It was also approved by the Human Research Ethics Committee of the University of Granada (968/CEIH/2019).

Instruments

The sociodemographic and obstetric data were gathered using a questionnaire that was completed by the participants during their pregnancy. The sociodemographic information was related to age, marital status, place of birth and country of origin, education level, and employment situation, among others. The obstetric data were related to the type of pregnancy (whether it was primiparous), number of previous children, etc.

Psychological evaluation of the mother

Perceived stress scale (PSS)

(Cohen et al., 1983; Remor, 2006). This scale evaluates the level of stress perceived during the last month. It is a self-report of 14 items with a five-point response scale (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = very often). In the Spanish version, the Cronbach's alpha coefficient of reliability was 0.81.

Prenatal distress questionnaire (PDQ)

(Caparros-Gonzalez et al., 2019; Yali & Lobel, 1999). The PDQ evaluates the concerns related to the specific stress of pregnancy. It addresses variables about the infant and her/his birth, child weight, the body image of the pregnant mother and her emotions and relationship with her child. It consists of 12 items, which are responded to through a 5-point Likert scale, from 0 (not at all) to 4 (extremely). In its Spanish version, the Cronbach's alpha coefficient was 0.74.

Evaluation of the children

Achenbach's child behavior checklist (CBCL)

(Achenbach & Rescorla, 2000). The CBCL was used in its version for children aged between 1 ½ and 5 years to evaluate the behavioral problems of the participants' children. This questionnaire asks the parents or guardians to mark 99 specific behaviors of the child and, in addition, they are allowed to include 3 more behaviors that they consider problematic and which are not in the list. The items are responded to in a Likert scale of 0 to 2 points (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true). It consists of scales for internalizing behaviors (Cronbach's alpha = 0.89), externalizing behaviors (Cronbach's alpha = 0.92) and total behaviors. It also contains other scales that contribute to the internalizing and externalizing scores and an additional stress scale.

Bayley's child development test-III (Bayley-III)

(Bayley, 2006). This test evaluates the cognitive, language and motor development of children aged 1–42 months. The cognitive

scale evaluates aspects such as visual preference, attention, memory, sensory-motor processing, exploration and manipulation, and concept formation. The language scale analyses the receptive and expressive language, and the motor scale assesses the fine and coarse motor skills. This test presents adequate internal validity, with a reliability coefficient ranging from 0.86 (in the fine motor subscale) to 0.91 (for coarse motor skills, cognition, and expressive communication); the remaining subscale of receptive language has a reliability coefficient of 0.87.

Evaluation of maternal cortisol

Hair cortisol concentrations

Chronic stress was evaluated through the analysis of cortisol in hair. This technique is noninvasive and enables a retrospective measurement of cortisol, from weeks to months. Moreover, it is not affected by the circadian fluctuation of cortisol, and the sample is kept at room temperature, with a long useful life (Greff et al., 2019). A lock of hair with approximately 150 hairs was collected from the participants, as close to the cranium as possible and from the back of the head (Sauvé et al., 2007). In order to determine the cortisol levels in the previous 3 months, coinciding with each trimester of pregnancy, 3 cm of each sample were analyzed (Stalder & Kirschbaum, 2012). All samples were kept at room temperature, wrapped in tin foil, to protect them from direct light and humidity, and they were analyzed by the Department of Pharmacology at the University of Granada. The analysis of the protocol is described in Romero-Gonzalez et al. (2018).

Procedure

Information was given to the participants about the study, during their first visit to the midwife, when they were briefed on the importance of this investigation and how it was going to be carried out. Those who agreed to participate read the information sheet and signed the informed consent form.

Next, a hair sample was collected for each participant, in order to analyze the cortisol concentration, and a new sample was collected in each trimester. Upon collection, the samples were immediately kept and marked with a code that was associated with the corresponding participant, which guaranteed their anonymity.

Furthermore, the participants completed the questionnaires online in each trimester of pregnancy through the Google Forms platform. These questionnaires included sociodemographic data (which were only gathered in the first contact), the PSS and the PDQ.

In the days prior to the child being 2 years old, the participants were contacted again, and a new hair sample was collected from them, following the previously explained protocol. In that moment, their children were also evaluated, with the CBCL, through an online form, and Bayley-III, by the same evaluator, at the Mind, Brain and Behaviour Research Centre of the University of Granada.

Data analysis

Firstly, we verified the assumptions of normality and homogeneity of variance through Shapiro-Wilk and Levene tests. However, the measurements of cortisol did not show a normal distribution, thus a logarithmic transformation was performed to adjust them to a normal distribution, following the analysis recommendations for this type of sample (Stalder & Kirschbaum, 2012).

Similarly, with the aim of analyzing the influence of stress throughout pregnancy on the neurodevelopment and behavior of

the children, we calculated the mean scores in PSS, PDQ, and hair cortisol of the three measurements recorded in each trimester.

To verify the existence of differences between the main sociodemographic and obstetric variables of the mothers of both groups, Student's t-tests and Chi-squared tests were performed for the continuous and categorical variables, respectively. On the other hand, to explore the differences in maternal stress and cortisol between groups, as well as in the neurodevelopment and behavior of their children at 24 months, new Student's t-tests were carried out.

Lastly, the effect size of the differences in neurodevelopment and cortisol was determined through Cohen's *d*, with the following values: $d \leq 0.20$ indicates a small effect size, $d \leq 0.50$ indicates a moderate effect size, and $d \leq 0.80$ indicates a large effect size (Cohen, 1988).

The analyses were conducted using Statistical Package for the Social Sciences 20.0 Macintosh v26 (SPSS, Armonk, New York, USA).

Results

Sample description

The 56 participants were divided into two groups according to the type of pregnancy: 27 women in the high-risk group ($M = 35.4$ years; $SD = 3.6$) and 29 in the low-risk group ($M = 33.7$ years; $SD = 3.2$).

Table 1 shows the main sociodemographic and obstetric variables of both groups. The results indicate that both groups had similar data in the sociodemographic and obstetric variables, since there were no differences between the groups in the analyzed variables.

Differences in the stress level, measured through questionnaires and hair cortisol, between high-risk and low-risk pregnant women

The comparison of the two groups shows that there were significant differences in the scores of perceived stress ($t = 2.17$; $p < .05$) and prenatal distress ($t = 2.15$; $p < .05$), with the high-risk women presenting higher scores in both scales with respect to the low-risk women. The effect size of the two scales was moderate ($d = 0.62$). No significant differences were found in the concentrations of cortisol in hair during pregnancy between the two groups (Table 2).

Table 3 shows the results of the analysis of maternal hair cortisol at 24 months, along with the evaluation of their children with Bayley-III and CBCL. The data show significant differences of maternal cortisol at 24 months after delivery ($t = -2.65$; $p < .05$), with the high-risk pregnancy group presenting lower maternal hair cortisol concentrations compared to the low-risk group, with a near-large effect size ($d = -0.73$).

Differences in neurodevelopment and behavior in offspring of high vs low-risk pregnancies

Regarding the children's scores, no differences were found between their ages. On the other hand, concerning the behavioral assessment, significant differences were found between the two groups in both externalizing and internalizing behaviors ($t = 2.06$; $p < .05$ and $t = -2.12$; $p < .05$, respectively). The children of the high-risk pregnant women presented a greater t score of internalizing behaviors, whereas the low-risk group obtained higher scores in externalizing behaviors. The effect size of both

Table 1. Differences in sociodemographic variables and obstetric information between high-risk and low-risk pregnant women

		High-risk (n = 27) M (SD)/n(%)	Low-risk (n = 29) M (SD)/n(%)	t/x	p
Sociodemographic variables					
Age		35.4(3.7)	33.7(3.2)	1.74	.09
Marital status	Married	16(72.7)	18(64.3)	5.11	.16
	Divorced	1(4.5)	-		
	Cohabitant	4(23)	3(35.7)		
Nationality	XXX	19(100)	26(92.9)	1.42	.35
	Immigrant	-	2(7.1)		
Level of education	Secondary school	9(40.9)	7(25)	1.43	.19
	University degree	13(59.1)	21(75)		
Employment situation	Unemployed	6(27.3)	8(28.6)	2.12	.71
	Employed	15(68.2)	20(71.4)		
	Studying	1(4.5)	-		
Tobacco consumption	No	21(95.5)	28(100)	1.30	.44
	Yes	1(4.5)	-		
Alcohol consumption	No	20(95.2)	28(100)	1.36	.43
	Yes	1(4.8)	-		
Obstetric information					
Primiparous	No	13(59.1)	15(53.6)	0.15	.46
	Yes	9(40.9)	13(46.4)		
Pregnancy method	Spontaneous	18(81.8)	23(82.1)	1.11	.58
	In vitro fertilization	4(18.1)	5(17.8)		
Baby sex	Masculine	13(54.2)	11(44)	0.51	.34
	Feminine	11(45.8)	14(56)		
Number of children	0	11(50)	15(53.6)	1.31	.52
	1	10(45.5)	13(46.4)		
	2	1(4.5)	-		
Previous miscarriages	0	9(40.9)	13(48.1)	2.07	.36
	1	5(22.7)	9(33.3)		
	2	8(36.4)	5(18.5)		
Reason of high-risk pregnancy diagnostic					
	Advanced maternal age	2(8.3)			
	Coagulation factors	6(25)			
	Hypothyroidism	1(4.2)			
	Genetic disorder	4(16.7)			
	Autoimmune disease	6(25)			
	Other	5(20.9)			

Note: Student t-tests were used to compare quantitative variables whereas chi-square tests for qualitative information.

behaviors was moderate ($d = 0.55$ and $d = 0.57$ for internalizing and externalizing behaviors, respectively).

In regard with the results of neurodevelopment assessed with Bayley-III, no significant differences were found in any of the subscales of this instrument.

Discussion

The aim of the present study was to verify the existence of differences in the stress level, measured as perceived stress, specific

pregnancy stress and hair cortisol concentration, between women with high-risk pregnancy and women with low-risk pregnancy, as well as to explore the possible differences in the neurodevelopment and behavior of their offspring at 24 months after delivery. The results showed that the levels of psychological stress were higher in the high-risk group, specifically perceived stress and distress related to specific pregnancy stress, detecting significant differences with respect to the low-risk group. These results are related to the characteristics of high-risk pregnancies, where mothers have multiple concerns related to the present and future health of

Table 2. Differences in maternal hair cortisol levels and psychological variables associated with pregnancy between high-risk and low-risk pregnancy

	High-risk <i>M (SD)</i>	Low-risk <i>M (SD)</i>	<i>t</i>	<i>p</i>	<i>d</i>
HCC	4.96(0.89)	4.79(1.12)	0.62	.54	0.17
PSS-14	25.47(6.28)	21.59(6.05)	2.17	.04	0.62
PDQ	16.91(4.96)	13.83(4.97)	2.15	.04	0.62

Note: HCC = Hair cortisol concentrations; PSS-14 = Perceived Stress Scale; PDQ = Prenatal Distress Questionnaire EEP.

Table 3. Comparison between groups of maternal hair cortisol levels and scores on behavior and neurodevelopment

			High-risk <i>M (SD)</i>	Low-risk <i>M (SD)</i>	<i>t</i>	<i>p</i>	<i>d</i>	
Maternal HCC 24 Months			4.55(0.90)	5.17(0.77)	- 2.65	.01*	- 0.73	
Child age (months)			24.08 (1.07)	24.64(1.62)	- 1.49	.13	- 0.34	
CBCL	Internalizing behavior	Total score	8.52(4.50)	7.62(9.47)	0.45	.66	0.12	
		T score	57.63(6.94)	53.69(7.34)	2.06	.04*	0.55	
	Externalizing behavior	Total score	13.26(5.34)	17.76(11.23)	- 1.89	.06	- 0.51	
		T score	58.30(7.11)	63.17(9.80)	- 2.12	.04*	- 0.57	
	Total problems	Total score	35(12.37)	37.52(14.23)	- 0.70	.48	- 0.18	
		T score	59.67(6.61)	61.21(8.12)	- 0.78	.44	- 0.22	
	Bayley-III	Cognitive	Total score	68.62(5.40)	69.68(6.33)	- 0.66	.51	- 0.20
			Scaled	13.42(3.13)	13.75(3.83)	- 0.34	.73	- 0.09
Composite			117.12(15.63)	118.75(19.13)	- 0.34	.73	- 0.08	
Language-Receptive communication		Total score	28.92(3.23)	29.96(5.48)	- 0.86	.40	- 0.27	
		Scaled	11.42(2.04)	11.89(3.28)	- 0.64	.53	- 0.15	
Language-Expressive communication		Total score	29.62(4.69)	31.07(5.26)	- 1.11	.27	- 0.28	
		Scaled	9.81(2.0)	10.61(2.70)	- 1.23	.23	- 0.31	
Language		Scaled	21.23(3.42)	22.50(5.55)	- 1.02	.31	- 0.22	
		Composite	103.81(10.1)	105.64(21)	- 0.41	.68	- 0.09	
		Percentile	58.15(22.29)	62.6(28.96)	- 0.63	.53	- 0.15	
Motor-fine	Total score	41.73(2.97)	41.29(2.69)	0.58	.57	- 0.15		
	Scaled	12.69(2.68)	11.89(2.1)	1.23	.23	0.29		
Motor-gross	Total score	59.04(4.47)	57.36(10.71)	0.74	.46	- 0.28		
	Scaled	12.77(4.26)	12.5(3.07)	0.26	.79	0.06		
Motor	Scaled	25.54(5.22)	24.39(4.46)	0.87	.39	0.22		
	Composite	116.65(15.66)	113.39(13.31)	0.83	.41	0.20		
	Percentile	78.21(23.79)	74.36(22.2)	0.62	.54	0.18		

Note: HCC = Hair cortisol concentrations.

themselves and that of their children, and they also usually experience contradicting emotions that alternate between happiness for the arrival of the baby and frustration and uncertainty (Holness, 2018).

Our results are in line with those reported by Rodrigues et al., (Rodrigues et al., 2016), who found that women with high-risk pregnancy had significantly higher stress levels and a worse emotional state than women with low-risk pregnancy. Moreover, it has been demonstrated that perceived stress in pregnant women predicts the obstetric risk and, therefore, is associated with greater complications in their health (Roy-Matton et al., 2011; Stark & Brinkley, 2007), which would have a greater negative impact on

high-risk pregnant women, since they already present severe pathologies. In this sense, it is very important to act jointly with health professionals and psychologists in the prevention and treatment of stress during pregnancy.

Surprisingly, psychological stress and cortisol showed different results. Despite the differences observed between the two groups in the levels of perceived stress, there were no differences in the concentration of maternal cortisol during pregnancy, which is in line with the results of a previous study, which found that the dysregulation of HPA is not related to the obstetric risk pregnancy (Romero-Gonzalez et al., 2020). In this line, different studies report that there is no consistent correlation between the concentration of

cortisol in maternal hair and the self-reports that evaluate psychological stress, due to different methodological and pathophysiological factors (Musana *et al.*, 2020; Mustonen *et al.*, 2018; Stalder *et al.*, 2017). However, the importance of analyzing hair cortisol concentration, as a biomarker of chronic stress, lies in the possibility of finding differences at the physiological level that can affect fetal programming in different ways (Mustonen *et al.*, 2018), although some studies state that the impact of prenatal stress on the offspring is not only influenced by maternal cortisol during pregnancy (Zijlmans *et al.*, 2015).

Regarding maternal stress and the behavioral problems of the children at 24 months after delivery, no significant differences were found between the two groups in terms of total behaviors, although there were significant differences in internalizing and externalizing behaviors, with the high-risk group obtaining higher scores in child internalizing behaviors, whereas the low-risk group presented higher scores in child externalizing behaviors.

These findings are very interesting, as few studies have analyzed the effects of high-risk pregnancy on the behavior of preschool children. Some studies have identified that different maternal risk factors, including smoking during pregnancy and having gestational hypertension, which are associated with stress during pregnancy, are more strongly related to behavioral problems in early childhood than to obstetric results (Tearne *et al.*, 2015). These data indicate that it is very important to research the influence of the prenatal environment on the offspring.

A previous study detected a direct relationship between prenatal maternal stress and internalizing symptoms of 5-year-old children in a low-risk sample (Hentges *et al.*, 2019). These data are consistent with the findings of our study and show that women with high-risk pregnancy need specialized care, as they have higher levels of perceived stress and distress related to the pregnancy compared to women with low-risk pregnancy, which not only affects them but also their offspring.

Internalizing behaviors are characterized by presenting symptoms that develop toward the interior of the individual. In this sense, there are different biological factors (regulation of the HPA axis, thyroid function, and levels of oxytocin, prolactin, and progesterone) and socio-psychological factors (insufficient social support, unplanned pregnancy, lack of physical activity, and high stress level) that allow explaining the negative impact of pregnancy-related anxiety on the mother and her child (Mikolajkow & Małyszczak, 2022); moreover, this type of stress is associated with rumination behavior, particularly negative repetitive thoughts, which increase the anxiety (Hirsch *et al.*, 2020).

Despite the above mentioned, these are controversial results, since a previous study reports that greater levels of perceived stress during pregnancy are related to greater externalizing behaviors in 27-month-old children (Gutteling *et al.*, 2005), although the authors assert that this relationship between stress and behavioral problems was not very strong in the analyzed sample.

Regarding the analysis of maternal stress at 24 months after delivery, measured through the concentration of hair cortisol, it was found that this parameter was higher in the low-risk group than in the high-risk group, which in turn showed greater externalizing behaviors. Given the temporality of the samples, we could assert that the relationship between maternal stress and the behavior of the children is bidirectional, since the stress of the mothers may cause behavioral problems in their children and, in turn, this behavior may cause maternal stress (Amici *et al.*, 2022). Thus, the externalizing symptoms could explain the increase of maternal hair cortisol at 24 months after delivery. The externalizing

behaviors of the children have a great impact on the environment, which can be highly stressful for the parents and guardians.

The dysregulation of the HPA axis and the increase of hair cortisol concentration can be due to the chronic exposure to stress (Stalder *et al.*, 2017). In this line, a study showed a relationship between the increase of maternal hair cortisol and how they interact with their children (Tarullo *et al.*, 2017). Therefore, other variables could be influencing the behavior of the children, such as upbringing styles and marital stress, which have been associated with externalizing behaviors (Schuetze *et al.*, 2020; Steenhoff *et al.*, 2021; Van Eldik *et al.*, 2017).

Lastly, in regard with the neurodevelopment of the children, no significant differences were found at 24 months after delivery between the high-risk and low-risk groups. These findings differ from those reported by Romero-Gonzalez *et al.* (2020), who obtained higher scores in motor, language, and cognitive development in the children of the high-risk group. This could be explained by the child age difference, as the mentioned authors analyzed a sample of 6-month-old babies, whose development may be more immediately and exclusively affected by the risk condition of pregnancy and dissipate in the long term, as was observed in our sample.

Other studies that explored the neurocognitive consequences of high-risk pregnancy due to chemotherapy treatment during gestation found no negative effects on the offspring, which is in line with the results of our study and demonstrates that, even in high-risk pregnancy, there are cases in which no maternal or fetal complications occur (Korakiti *et al.*, 2020). Moreover, it is worth mentioning that high-risk pregnancy involves specialized medical care, which contributes to improving the health of these pregnant women to prevent complications, and this could favor the neurodevelopment of their children (Ringholm *et al.*, 2019).

The present study provides data about the influence of high-risk pregnancy on the neurodevelopmental and behavioral problems of the offspring, compared with low-risk pregnancy. Since research in this topic is scarce, this study shows novel results. However, the main limitations of this work are related to the sample size, which was small and prevented us from delving into the types of pathologies that could explain our findings.

Future studies should expand the sample size and follow up the results in different ages, analyzing, in addition, the potential mediator role of different upbringing styles, the duration of breastfeeding and the attachment style in neurodevelopmental and behavioral problems of the offspring, as well as the different factors that may act as buffers of prenatal stress. Moreover, it would be even more interesting to include hospitalized women with high-risk pregnancy, since, as was observed, this condition is an additional source of prenatal stress. Considering the relation found between maternal hair cortisol at 24 months postpartum and child externalizing behavior, it would be interesting to assess this type of measure on the other parent, if any, to study the impact of both parents on the child's behavior. Finally, another line of study could be to analyze the different symptoms of internalizing behavior present in children born from high-risk pregnancies and explore if these are related to other variables of interest mentioned above.

In conclusion, this study has important clinical implications, as it provides data that demonstrate the importance of taking care of pregnant women's health, not only from the physical point of view, but also from the psychological perspective. It was found that the women with high-risk pregnancy had higher perceived stress and greater pregnancy-related distress than the women with low-risk pregnancy. Furthermore, the children of the high-risk women obtained higher scores in internalizing behaviors compared to

those of the low-risk women, who had higher scores in externalizing behaviors. In addition, greater maternal hair cortisol concentrations at 24 months after delivery were found in the low-risk group.

These findings highlight the need for designing stress detection and prevention programs, from early stages of pregnancy, in order to improve the health of the mother and that of the future child, especially in high-risk pregnancy. It is also important for healthcare professionals to be sensitized with the psychological characteristics of the diagnosis of high-risk pregnancy and their impact on the mothers, which can reduce their stress levels, thereby benefiting the mothers and their offspring.

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Competing interests. None.

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