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**Research** Paper

# Pregnancy and mental health outcomes during the COVID–19 pandemic in Colombia: A nationwide cross-sectional study



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## 1. Introduction

The SARS-CoV-2 virus has spread across the world since late December 2019, generating a worldwide pandemic. However, COV-ID-19 pandemic had an unequal disease burden, causing unprecedented health and socioeconomic crises in high, middle, and low-income countries (Werner et al., 2020). The burden of COVID-19 extends far beyond that of a contagious disease. While respiratory disorders were the main concern at the beginning of the pandemic, other important clinical domains have also been compromised because of the SARS-CoV-2 infection. Thus incidence rates of cardiovascular (Long et al., 2020), inflammatory (Zeng et al., 2020), neurological, (Ellul et al., 2020; Mackenzie et al., 2021) metabolic, (Puig-Domingo et al., 2020) and mental disorders have also risen (Wang et al., 2021; Talevi et al., 2020). Previous studies have reported several mental outcomes in patients during and after COVID-19 infection (Winkler et al., 2020; Xiong et al., 2020). Pregnant women represent a population at a higher risk for adverse mental outcomes during the COVID-19 pandemic. Previous studies have reported that several mental disorders such as anxiety (Goodman et al., 2014), depression (Lancaster et al., 2010), post-traumatic stress disorder (PTSD) (Yildiz et al., 2017), insomnia (Sedov et al., 2021), among others, are common during pregnancy (Jha et al., 2018).

At this point, a high level of psychosocial adversities has also been generated for pregnant women during the COVID 19 pandemic (Werner et al., 2020; Burki, 2020; Parra-Saavedra and Miranda, 2021; Parra--Saavedra et al., 2020). These have included prolonged lockdowns and quarantine restrictions, high levels of unemployment, economic decline, changes in healthcare access an emerging, and continued fear of contagion in minorities and underserved population (Werner et al., 2020; Burki, 2020; Roberton et al., 2020). Consequently, a noticeable reduction of expected healthcare-seeking behaviors in pregnant women and higher levels of mood symptoms have been reported elsewhere (Khalil et al., 2021; Raiff et al., 2022). Furthermore, an increase in maternal mortality, stillbirth, ruptured ectopic pregnancies, and maternal stress during the COVID-19 pandemic have also been reported (Chmielewska et al., 2021). The association between mental disorders and pregnancy also has been reported mainly in high-income countries (Parra-Saavedra et al., 2020; López-Morales et al., 2021b; Wu et al., 2020). Various longitudinal studies evaluating maternal-offspring's outcomes with COVID-19 exposure in High Income Countries such as SIGNATURE study (Garrido-Torres et al., 2022) in Spain, the Pregnancy During the COVID-19 pandemic (PdP) (Giesbrecht et al., 2021) in Canada, and MOM-COPE study in Italy are currently being developed, however, fewer studies have explored this association in low- and middle-income countries (LMICs) for pregnant women during the

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COVID-19 pandemic (López-Morales et al., 2021a, 2021b). Thus, we decided to pursue a nationwide cross-sectional study in Colombia with three main objectives. First, explore the prevalence of PTSD, anxiety, depression, and insomnia symptoms in pregnant women during the pandemic. The second, was to describe the severity of specific symptom domains in mental disorders, and the third was to identify possible associated factors between the development of mental outcomes such as PTSD, anxiety, depression, and insomnia symptoms with adverse pregnancy outcomes.

## 2. Material and methods

## 2.1. Study design

A multi-center cross-sectional web-survey study was carried out, including 721 pregnant women during follow-up in six academic teaching hospitals/private clinics across six cities in Colombia (Barranquilla, Bogota D.C., Bucaramanga, Cartagena, Ibague, and Pereira). Clinicians directly involved in antenatal care of patients were e-mailed a link for an internet-based questionnaire (available in Spanish) that was designed using the online tool *Google forms*. All data was collected and registered in an independent account with exclusive access to the researcher running the analyses. The STROBE statement (von Elm et al., 2007) and Good Clinical Practices were followed accordingly. After explaining the nature of the study, participants signed a written consent form, and the Ethics Committee from Universidad Simon Bolivar approved the study protocol.

## 2.2. Participants

Pregnant women in the first, second, and third trimesters were openly invited to participate and complete the web-survey during their regular obstetric consultations. A total of 721 pregnant women completed the web-survey and evaluations to a convenience sample. The target sample size was calculated using the formula  $N = Z_a^2 P(1-P)/d^2$ , in which  $\alpha = 0.05$  and  $Z_{\alpha} = 1.96$ , and the estimated margin of error for proportion *d* was 0.1. We used the proportion of anxiety symptoms in pregnant women during the COVID-19 pandemic since it is a higher value compared with PTSD, depression, and insomnia symptoms. The proportion used was 42%, according to the meta-analysis by Fan et al. (2021) A total target population of 93 pregnant women was calculated to obtain an adequate estimation. Fortunately, we were able to increase our sample size up to a total of 721 women participants.

## 2.3. Survey

The survey was open between September 2021 and November 2021 to obtain the required sample size and consisted of questions with multiple-choice answers and Likert scale formats. The survey was carryout during the third wave in Colombia without lockdown restrictions in the country. During this time, Colombia reported more than 4.9 million of cases of COVID-19. The higher rates of cases were in Bogota D.C, Barranquilla, Bucaramanga, Cartagena, Pereira and Ibague. The survey covered questions to collect sociodemographic, clinical, and psychometric variables. In addition, questions assessing scales for mental health were performed.

## 2.4. Psychometric scales

## 2.4.1. PCL - 5

The Post-traumatic Stress Disorder Checklist (PCL-5) for DSM-5 is a 20-item self-report measure in symptoms related to PSTD according to DSM-V criteria. The scale is a 5-point Likert type, and participants are asked to rate the severity of their experiences (Blevins et al., 2015). Previous studies in pregnant women had used PCL-5 (Kara et al., 2021). A cutoff point of  $\geq$ 33 was indicative of probable PTSD (Blevins et al.,

2015). A total symptom severity score range between 0 and 80 points. The Cronbach's value of this study was 0.92.

## 2.4.2. GAD - 7

7-item Generalized Anxiety Disorder Scale is a useful tool for screening anxiety symptoms and probable cases of General Anxiety Disorder (GAD) (Spitzer et al., 2006). Previous studies have validated the GAD-7 scale for pregnant women (Zhong et al., 2015). The cutoff point was fixed in  $\geq$ 5 according to Spitzer et al. (2006) The Cronbach's value of this study was 0.86.

## 2.4.3. PHQ - 9

The 9-items Patient Health Questionnaire is a scale designed to screen depression symptoms in the general population (Kroenke et al., 2001). PHQ - 9 has a good internal consistency (Cronbach's value > 0,8), and previous studies had validated the PHQ - 9 for antepartum depression assessment (Zhong et al., 2014). The cutoff point of  $\geq$ 7 was considered according to previous studies on Colombia population (Cassiani-Miranda et al., 2021). The Cronbach's value of this study was 0.87.

## 2.4.4. ISI

The Insomnia Severity Index is an instrument designed to assess the severity of insomnia with excellent internal consistency (Cronbach's value > 0.90). Previous studies had evaluated the ISI scale for screening insomnia symptoms during pregnancy (Sedov et al., 2021). A cutoff value of  $\geq$ 10 was optimal for detecting insomnia cases according to Morin et al. (2011) In our study, the Cronbach's value was 0.91.

## 2.5. Ethical consideration

This study followed the ethical principles for medical research involving human subjects in the Declaration of Helsinki and The Council for International Organizations of Medical Sciences (CIOMS). All participants signed a written consent form, and the Ethics Committee from Universidad Simon Bolivar approved the study protocol.

## 2.6. Statistical analysis

Statistical analysis was conducted using Stata v17 SE-Standard Edition (Stata Corp LLC, College Station, TX). Univariate and bivariate analyses were performed; continuous variables were presented as means and standard deviations or median and interquartile ranges (IQRs) as appropriate. Categorical variables were presented as frequency and percentage. Chi-square or Fisher exact tests were used for categorical variable analyses. Also, Mann-Whitney U and Kruskal Wallis Tests were applied to variables with non-normal distribution. Four multivariate logistic regression models were created for PCL - 5, GAD - 7, PHQ - 9, and ISI scores according to the cutoff values set. In the above scenario, we aimed to identify associated risk factors with developing mental health symptoms in pregnant women. The models were adjusted for potential confounders such as age, gender, marital status, socioeconomic status, education, employability, ethnicity, weeks of pregnancy, obstetric conditions -any physical or mental condition during pregnancy-, and previous diagnosis of SARS-CoV2 infection during the last 12-months. Model assumptions were validated through a linearity test, the Hosmer-Lemeshow test, an estimation of deviance residuals and Cook's values, and a comparison between the crude and the adjusted models. All probability values were 2 - tailed, the error alpha was = 0.05, and a 95% confidence interval (CIs).

## 3. Results

An overall of 721 pregnant women were included in this study. The mean maternal age was  $27 \pm 5.82$  years. The demographic characteristics of the study population are shown in Table 1. The prevalence of

#### Table 1

Demographic characteristics	in	pregnant	women.
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Demographic Characteristics of P Quantitative Variables	articipants ( $n = 721$ (Mean $\pm$ SD)	) Minimum	Maximum
Age	$27 \pm 5,82$	14	43
Pregnancy (weeks)	$21,9\pm8,47$	4	41
Score PCL-5	7,4 $\pm$ 9,5	0	65
Score GAD-7	$3,1\pm3,6$	0	21
Score PHQ-9	$3,3\pm3,8$	0	25
Score ISI	$4,9 \pm 5,2$	0	28
Categorical Variables			F (%)
Age by groups			
18–24			268 (37,17)
25–34			362 (50,21)
≥35			91 (12,62)
Marital status			
Single			114 (15,81)
Married			607 (84,19)
Socioeconomic			
Low			551 (76,42)
Middle			157 (21,78)
High			13 (1,80)
Education			
Elementary			23 (3,19)
High School			289 (40,08)
Technical			241 (33,43)
Graduate			124 (17,20)
Postgraduate			44 (6,10)
Ethnic			
Hispanic			516 (71,57)
Afro-Colombian			75 (10,41)
Indigenous			44 (6,10)
Other			86 (11,92)
Occupation			
Employment			355 (49,24)
Unemployment			366 (50,76)
Previous COVID-19 diagnosis	:		
Yes			104 (14,42)
No			617 (85,58)
Obstetric Conditions			
Yes			168 (23,30)
No			553 (76,70)
Hypertension			50 (6,93)
Diabetes			32 (4,44)
Threatened Preterm Labor			29 (4,02)
Intrauterine Growth Restriction			27 (3,74)
Metabolic-related			17 (2,36)
Immune-related			7 (0,97)
Infectious			11 (1,53)
Pregnancy Trimester			
First			194 (26,91)
Second			322 (44,66)
Third			205 (28,43)

PCL—5: Post-traumatic Stress Disorder Checklist for DSM-5; GAD-7: 7-items Generalized Anxiety Disorder Scale; PHQ-9: 9-items Patient Health Questionnaire Scale; ISI: Insomnia Severity Index Scale; SD: Standard Deviation.

mental disorders among the study population was 2.77% for PTSD, 27.88% for anxiety, 14.70% for depression, and 16.50% for insomnia symptoms (Table 2). The mean PTSD score in the sample was  $4 \pm 9,50$ . A relation between independent factors such as age ( $\chi$  (Long et al., 2020)

= 9.90, df = 2, p = .007), education ( $\gamma$  (Long et al., 2020) = 16.90, df =4, p = .002), any obstetric condition ( $\chi$  (Long et al., 2020) = 8.20, df = 1, p = .004) were identified with positive PTSD symptoms. The GAD - 7 score had a median of  $2 \pm 3.57$  SD in the sample. Our findings suggest a relation between positive symptoms of anxiety and any obstetric condition ( $\chi$  (Long et al., 2020) = 8.87, df = 1, p = .002) and threatened preterm labor (TPL) ( $\gamma$  (Long et al., 2020) = 8.54, df = 1, p = .003). The PHQ - 9 score had a mean of 2  $\pm$  3.79 SD in the sample. Depressive symptoms showed a relation with TPL ( $\chi$  (Long et al., 2020) = 6.42, df = 1, p = .011) in the sample. The score in the ISI scale had a mean of 3  $\pm$ 5.16 SD in the sample. Insomnia symptoms were associated with any obstetric condition ( $\chi$  (Long et al., 2020) = 18.80, df = 1, p < .001), TPL ( $\chi$  (Long et al., 2020) = 10.06, df = 1, p = .002), intrauterine growth restriction (IUGR) ( $\chi$  (Long et al., 2020) = 11.95, df = 1, p = .001), metabolic disorders (thyroid disorders, metabolic syndrome or obesity)  $(\chi \text{ (Long et al., 2020)} = 4.46, df = 1, p = .03)$  (Table 3).

Related to severity symptoms, 22.61%, 3.47%, and 1.80% of pregnant women showed mild, moderate, and severe anxiety symptoms, respectively. Regarding to severity depressive symptoms, the 20.11%, 4.16%, 0.97%, and 0.97% of pregnant women shown mild, moderate, moderately severe, and severe depression symptoms, respectively. On the other hand, the 20.25% had a subthreshold insomnia, 4.72% and 1.11% of pregnant women shown moderate and severe insomnia symptoms, respectively (Table 3).

Finally, four multivariable logistic regression analyses were adjusted for potential confounders. The first model for PTSD identified that, being a pregnant woman and having an obstetric condition were associated with probable PTSD (OR = 2.95; 95% CI 1.18–7.34; p = .02). Additionally, being a pregnant woman and having  $\geq$ 35 years were associated also with probable PTSD (OR = 5.31; 95% CI, 1.47–19.19; p = .01). Likewise, the anxiety model showed that having an obstetric condition was associated with positive anxiety symptoms compared with woman without obstetric conditions (OR = 1.56; 95% CI, 1.03-2.35; p = .03). Another important finding is, being a pregnant woman and suffering from unemployment during the pandemic was associated with positive anxiety symptoms (OR = 1.47; 95% CI, 1.01–2.13; *p* < .04). In that same line of thought, the depression model showed a positive association with being pregnant, having a threat of preterm labor and significant depressive symptoms (OR = 3.02; 95% CI, 1.12-8.17; p = .03) during the pandemic. Furthermore, unemployed pregnant women have 65% more probability to suffer from significant depressive symptoms during in COVID-19 pandemic compared with those pregnant women who continue to be employed (OR = 1.65; 95% CI, 1.02-2.66; p = 0.04). As pregnancy progressed in time, there seems to be a protective factor for depressive symptoms (OR = 0.95; 95% CI, 0.92–0.97; p < .001). With regards to insomnia and sleep problems model, the model showed that pregnant women with TPL had a higher association with insomnia symptoms (OR = 2.53; 95% CI, 1.09–5.85; p = .03). Pregnant woman with IUGR also has an important association with insomnia symptoms during the pandemic (OR = 3.82; 95% CI, 1.67-8.71; p < .001) (Table 4).

## Table 2

Prevalence of mental health outcomes in pregnant women.

		PTSD (PCL-	-5)	Anxiety (GAD	-7)	Depression (P	HQ-9)	Insomnia (ISI)	)
	Overall, n (%)	Yes $\geq$ 33	No <33	Yes $\geq 5$	No <5	Yes ≥7	No <7	$\substack{ \text{Yes} \\ \geq 10 }$	No <10
Frequency of Symptoms, n (%)	721 (100)	20 (2,77)	701 (97,23)	201 (27,88)	520 (72,12)	106 (14,70)	615 (85,30)	119 (16,50)	602 (83,50)

PTSD: Post-traumatic stress disorder; PCL-5: Post-traumatic stress disorder Check-list for DSM-5.

GAD-7: 7-item Generalized Anxiety Disorder Scale.

PHQ-9: 9-item Patient Health Questionnaire Scale.

ISI: Insomnia Severity Index Scale.

Table 3	
Mental Health Outcomes and Factors Related to Pregnant Women.	

Variables	PCL-5				GAD-7				PHQ-9				ISI			
	<33	$\geq$ 33	overall	p value	<5	$\geq$ 5	overall	p value	<7	≥7	overall	p value	<10	$\geq 10$	overall	p valu
Age																
<25	264 (98,51)	4 (1,49)	268 (100)	.007	198 (73,88)	70 (26,12)	268 (100)	.243	227 (84,70)	41 (15,30)	268 (100)	.136	229 (85,45)	39 (14,55)	268 (100)	.435
25–34	353 (97,51)	9 (2,49)	362 (100)		263 (72,65)	99 (27,35)	362 (100)		316 (87,29)	46 (12,71)	362 (100)		300 (82,87)	62 (17,13)	362 (100)	
≥35	84 (92,31)	7 (7,69)	91 (100)		59 (64,84)	32 (35,16)	91 (100)		72 (79,12)	19 (20,88)	91 (100)		73 (80,22)	18 (19,78)	91 (100)	
															. ,	
Single	108 (94,74)	6 (5,26)	114 (100)	.078	77 (67,54)	37 (32,46)	114 (100)	.255	93 (81,58)	21 (18,42)	114 (100)	.222	96 (84,21)	18 (15,79)	114 (100)	.823
Married	593 (97,69)	14 (2,31)	607 (100)		443 (72,98)	164 (27,02)	607 (100)		522 (86,00)	85 (14,00)	607 (100)		506 (83,36)	101 (16,64)	607 (100)	
Socioeconomic	()/,0))	(2,31)	(100)		(72,90)	(27,02)	(100)		(00,00)		(100)		(03,30)	(10,04)	(100)	
Low	537	14	551	.267	406	145	551	.210	474	77 (13,97)	551	.434	469	82 (14,88)	551	.082
Middle	(97,46) 152	(2,54) 5 (3,18)	(100) 157	.207	(73,68) 105	(26,32) 52 (33,12)	(100) 157	.210	(86,03) 131	26 (16,56)	(100) 157	.101	(85,12) 123	34 (21,66)	(100) 157	.002
Wilddie		5 (3,18)	(100)		(66,88)	52 (55,12)	(100)		(83,44)	20 (10,30)	(100)		(78,34)	34 (21,00)	(100)	
High	(96,82) 12 (92,31)	1 (7,69)	(100) 13 (100)		(66,88) 9 (69,23)	4 (30,77)	(100) 13 (100)		(83,44) 10 (76,92)	3 (23,08)	(100) 13 (100)		(78,34) 10 (76,92)	3 (23,08)	(100) 13 (100)	
Education	01 (01 00)	0 (0 50)	00 (100)	000	10 (70.00)	5 (01 5 4)	00 (100)	005	00 (00 00)	0 (10 04)	00 (100)		00 (00 00)	0 (10 0.0)	00 (100)	0.0
Elementary	21 (91,30)	2 (8,70)	23 (100)	.002	18 (78,26)	5 (21,74)	23 (100)	.225	20 (86,96)	3 (13,04)	23 (100)	.784	20 (86,96)	3 (13,04)	23 (100)	.069
High School	285	4 (1,38)	289		211	78 (26,99)	289		248	41 (14,19)	289		250	39 (13,49)	289	
T	(98,62)	0 (1 0 4)	(100)		(73,01)	(1 (05 01)	(100)		(85,81)	00 (10 (0)	(100)		(86,51)	07 (15 05)	(100)	
Technical	238	3 (1,24)	241		180	61 (25,31)	241		208	33 (13,69)	241		204	37 (15,35)	241	
Graduate	(98,76) 115	9 (7,26)	(100) 124		(74,69) 85 (68,55)	39 (31,45)	(100) 124		(86,31) 101	23 (18,55)	(100) 124		(84,65) 94 (75,81)	30 (24,19)	(100) 124	
	(92,74)		(100)				(100)		(81,45)		(100)				(100)	
Postgraduate Previous COVID-19 diagnosis	42 (95,45)	2 (4,55)	44 (100)		26 (59,09)	18 (40,91)	44 (100)		38 (86,36)	6 (13,64)	44 (100)		34 (77,27)	10 (22,73)	44 (100)	
No	602	15	617	.190	448	169	617	.480	532	85 (13,78)	617	.099	520	97 (15,72)	617	.16
	(97,57)	(2,43)	(100)		(72,61)	(27,39)	(100)		(86,22)		(100)		(84,28)		(100)	
Yes	99 (95,19)	5 (4,81)	104 (100)		72 (69,23)	32 (30,77)	104 (100)		83 (79,81)	21 (20,19)	104 (100)		82 (78,85)	22 (21,15)	104 (100)	
Obstetric Condition																
No	543	10	553	.012	414	139	553	.004	479	74 (13,38)	553	.069	480	73 (13,20)	553	.00
	(98,19)	(1,81)	(100)		(74,86)	(25,14)	(100)		(86,62)		(100)		(86,80)		(100)	
Yes	158	10	168		106	62 (36,90)	168		136	32 (19,05)	168		122	46 (27,38)	168	
ni	(94,05)	(5,95)	(100)		(63,10)		(100)		(80,95)		(100)		(72,62)		(100)	
Threatened Preterm Labor	674	10	692	.190	500	186	(00)	.006	505	07 (14 00)	692	.011	584	108	692	.00
No	674 (97,40)	18 (2,60)	692 (100)	.190	506 (73,12)	(26,88)	692 (100)	.006	595 (85,98)	97 (14,02)	(100)	.011	584 (84,39)	(15,61)	(100)	.00
Yes	27 (93,10)	2 (6,90)	29 (100)		14 (48,28)	15 (51,72)	29 (100)		20 (68,97)	9 (31,03)	29 (100)		18 (62,07)	11 (37,93)	29 (100)	
Intrauterine Growth Restriction		.,,,														
No	675	19	694	.539	504	190	694	.131	594	100	694	.261	586	108	694	.00
	(97,26)	(2,74)	(100)		(72,62)	(27,38)	(100)		(85,59)	(14,41)	(100)		(84,44)	(15,56)	(100)	
Yes	26 (96,30)	1 (3,70)	27 (100)		16 (59,26)	11 (40,74)	27 (100)		21 (77,78)	6 (22,22)	27 (100)		16 (59,26)	11 (40,74)	27 (100)	
Pregnancy Trimester			/		, . ,		/			. , ,				, ,		
First	187	7 (3,61)	194	.568	143	51 (26,29)	194	.273	156	38 (19,59)	194	.091	163	31 (15,98)	194	.37
	(96,39)	.,,	(100)		(73,71)		(100)		(80,41)		(100)		(84,02)		(100)	
Second	315	7 (2,17)	322		238	84 (26,09)	322		281	41 (12,73)	322		274	48 (14,91)	322	
	(97,83)		(100)		(73,91)		(100)		(87,27)		(100)		(85,09)		(100)	
Third	199	6 (2,93)	205		139	66 (32,20)	205		178	27 (13,17)	205		165	40 (19,51)	205	
-	(97,07)	. (=,- 0)	(100)		(67,80)		(100)		(86,83)	, (,-/)	(100)		(80,49)		(100)	

PTSD: Post-traumatic stress disorder; PCL-5: Post-traumatic stress disorder Check-list for DSM-5.

GAD-7: 7-item Generalized Anxiety Disorder Scale.

PHQ-9: 9-item Patient Health Questionnaire Scale.

ISI: Insomnia Severity Index Scale.

4

#### Table 4

Multivariate Lo	ogistic Mode	l to Mental	Disorder	rs in Pregnant	Women.

ē			U		
	OR	aOR	95% C		p value
PTSD			Min	Max	
Pregnancy Health Conditions					
No	1 [Ref	erence]	N/A		0,02
Yes	3,43	2,95	1,18	7,34	
Age					
18–24	1 [Ref	erence]	N/A		0,01
≥35	5,49	5,31	1,47	19,19	
Anxiety					
Pregnancy Health Conditions					
No	1 [Ref	erence]	N/A		0,03
Yes	1,74	1,56	1,03	2,35	
Occupation					
Employment	1 [Ref	erence]	N/A		0,04
Unemployment	1,14	1,47	1,01	2,13	
Depression					
Occupation					
Employment	1 [Ref	erence]	N/A		0,03
Unemployment	1,25	1,65	1,02	2,66	
Threatened Preterm Labor					
No	1 [Ref	erence]	N/A		0,03
Yes	2,76	3,02	1,12	8,17	
Weeks of Pregnancy	0,97	0,95	0,92	0,97	< 0,001
Insomnia					
Threatened Preterm Labor					
No	1 [Ref	erence]	N/A		0,03
Yes	3,3	2,53	1,09	5,85	
Intrauterine Growth Restriction					
No	1 [Ref	erence]	N/A		< 0,001
Yes	3,73	3,82	1,67	8,71	

PTSD: Post-traumatic Stress Disorder; OR: Odds Ratio; aOR: adjusted Odds Ratio; CI: Confidence Interval.

#### 4. Discussion

This study is the first to analyze mental outcomes in pregnant women during an environmental exposure as the COVID – 19 pandemics in Colombia. Pregnant women with having any obstetric condition were strongly associated with probable PTSD, and anxiety symptoms. Specifically, having a TPL shows a strong association with depressive and insomnia symptoms. Another important obstetric condition as IUGR evidence also a strong association with insomnia symptoms. Demographic factors such as unemployment pregnant women showed association with anxiety and depression symptoms. There was not association identified with pregnancy trimester or previous SARS-CoV2 infectious with the mental health outcomes assessed. Those clinical and demographic findings identified in a nationwide sample of pregnant women in Colombia are important in the context of a middle and low socioeconomic setting.

Previous studies had reported prevalence of PTSD in pregnant women ranged from 3.3% to 18.95% with differences between community samples and high-risk samples (Guillén-Burgos and Gutiérrez-Ruiz, 2018). Community samples have lower proportion than samples of pregnant women with obstetric conditions (Yildiz et al., 2017). In our study, we reported a prevalence of probable PTSD in pregnant women without obstetric conditions lower (2.20%) than the prevalence of PTSD symptoms in pregnant women with any obstetric condition (5.95%) ( $\chi^2 = 8.20$ , df = 1; p = .004). Other studies had reported a higher prevalence and more symptoms of PTSD in pregnant women than pregnant women in the pre-COVID – 19 sample (Liu et al., 2021; Berthelot et al., 2020).

Tomfohr-Madsen et al. (2021) shows a prevalence of anxiety in pregnant women of 30.5%. Our results show a point prevalence of 27.8% closely to the pooled prevalence evidenced in the meta-analysis (Tomfohr-Madsen et al., 2021). TPL has been associated to anxiety in previous published studies (Dayan et al., 2002). In our findings, TPL shows in 51.72% (15/29) of pregnant women having positive symptoms above of the cutoff point in the GAD-7 scale ( $\chi^2 = 8.54$ ; p < .003).

Unemployment status also has been assessed as sociodemographic risk factor to mental outcomes. Anxiety and others mental symptoms are been associated with unemployment status compared to people with stable job (Linn et al., 1985). Our model shows that there are 47% of probability to explore anxiety symptoms during pregnancy if the women are unemployed. This is a crucial circumstance in low-and-middle-income countries where the unemployment rates are highest even more, the inequity between men and women searching jobs.

Tomfohr-Madsen et al. (2021) also reported a pooled prevalence of depression in pregnant women of 25.6%. Our results are lower (14.70%) than the results evidenced in the meta-analysis, however, exist a heterogeneity between studies analyzed according to the scales used during the evaluation. Not all the studies used the PHQ – 9 and there are differences between results in the psychometric instruments. Previous studies have showed odds ratios ranged between 1.08 and 2.01 associating to preterm birth with depressive symptoms in pregnant women (Männistö et al., 2016; Liu et al., 2016; Venkatesh et al., 2016). We reported a 3-fold increased risk of being pregnant women with TPL and having depressive symptoms. Dagklis et al. (2017) reported that one quarter of the pregnant women hospitalized due to TPL were depressed. Thoughts of abortion were associated with risk of depression in this cohort of pregnant women (Dagklis et al., 2017).

Pregnant women are more likely to suffer from different sleep disorders such as insomnia, poor sleep quality, restless legs syndrome, and obstructive sleep apnea (Pien and Schwab, 2004; Lu et al., 2021; Zhou et al., 2020). In Demissie and Bitew (2021) shown a pooled prevalence of insomnia of 33.53% in pregnant women. We reported a point prevalence in our cohort of women of 16.50% insomnia symptoms during COVID-19 pandemic. In a previous published study by our research team, we reported a 49.1% of insomnia symptoms in a nationwide cohort of pregnant women (Parra-Saavedra et al., 2020). However, the differences in the estimated prevalence between the previous study and the current are mediated by the instrument used. Furthermore, IUGR has a higher incidence in LMCIs than high income countries (Sharma et al., 2016). Little attention has been IUGR with insomnia symptoms in pregnant women. Deprivation of sleep has been associated with low birth weight with a odds ratio of 2.84 (Abeysena et al., 2010). We reported a higher odds ratio of 3.82 than the study published by Abeysena et al. (2010).

It is well know that females present an increased risk of PTSD compared than males (Tolin and Foa, 2008). A large cohort of follow-up shows that adverse levels of maternal utero proinflammatory cytokines impact brain development of offspring's in a sexual dimorphic manner that persists across the lifespan with an increased risk of stress-related disorders (Goldstein et al., 2021). Additionally, several factors (obstetrics, hormonal, psychiatric, and social) have been also associated with increased PTSD risk during pregnancy (Kara et al., 2021). Also, having PTSD symptoms during pregnancy are at increased risk of excessive behaviors such as alcohol and substance use, smoking, and poor prenatal care. Those high-risk behaviors are involved in negative perinatal outcomes.

Studies suggest that progesterone is essential to maintaining the pregnancy (Pařízek et al., 2014) and vaginal progesterone's reduce the risk to preterm labor (Romero et al., 2012). However, progesterone activity in the brain also has been associated with the anxiety circuit (Salim et al., 2012). Therefore, are disparities in whether progesterone is the mechanism or pathway to stimulate anxiety symptoms in pregnant women. Although inflammatory mechanisms are more associated with preterm labor, the neuroendocrine mechanisms also have been linked to anxiety symptoms. Furthermore, high level of IL – 6 has been identified as an inflammatory response to anxiety and inside of the inflammatory cascade during preterm labor. Maternal immune activity during pregnancy also has been linked to risk for psychiatric disorders in offspring, considering pregnancy as an sensitive period of women life and important for child development (Yu et al., 2020). It is worth noting that

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the full biological mechanisms to explain the full term and preterm labor are still under research.

The neurobiological process between depression and preterm birth are still unclear. The stress response mediated by Hypothalamic-Pituitary-Adrenal Axis (HPA) with an increased level of glucocorticoids and proinflammatory cytokines implicated in the onset of parturition has been also vinculated in the neurobiological mechanisms of depression according to studies published (Shenassa et al., 2021). Besides, different periods in the lifespan such as pregnancy and menopausal transition have significant implications related to steroid hormones in Major Depression Disorder (Goldstein et al., 2014). However, pathophysiological pathways underpinning the association between depression and preterm birth still in research study.

Pro-inflammatory cytokines such as interleukin – 6 (IL – 6) and tumor necrosis factor- $\alpha$  (TNF -  $\alpha$ ) in the brain network are involved in sleep disorders (Krueger, 2008; Irwin and Opp, 2016). Those cytokines also has been linked to preterm labor. We identified a positive association between TPL with insomnia severity. These clinical findings are consistent with the biological approach proposal to preterm labor and insomnia reported.

Another important aspect related to obstetric disorders is the prenatal maternal infection and neuropsychiatric disorders in offspring's where evidence suggest the activation of immune-inflammatory response during maternal infection and risk of abnormal fetal brain development. In this sense, is important to clarify the underlying mechanisms related to infection-induced maternal immune activation and the role of theses markers in the development of neuropsychiatric conditions in the COVID-19 framework (Ayesa-Arriola et al., 2021).

Our study shows strengths as strong association in a large Colombian sample of obstetric conditions in pregnant women with mental health outcomes during COVID-19 in Colombia were identified. These results are consistent with epidemiological studies, and supported by biological approaches previously published. Also, we have limitations related to the study design trying to identify causality. Second, we do not use methods to calculate a probabilistic sample. Third, our outcomes were measured with self-administered screening tools and as we know, false positives could be present. Fourth, the prevalence for any mental disorder during pregnancy are still uncertain, making difficult the comparison about our results with previous data in this context (Mojica-Perilla et al., 2019).

## 5. Conclusions

Our results can conclude that obstetric conditions and sociodemographic factors are associated with PTSD, anxiety, depression and insomnia symptoms in Colombian pregnant women. These possible risk factors have been identified previously in studies in high income countries, however little is known about the role of those factors in lowand middle-income countries. Difference in pregnant outcomes across countries have been described and the relevance of these findings are supported by the context of a low-and-middle country during an environmental exposure as COVID-19 pandemic. In context of maternal-fetal controls of pregnant women is important the screening of mental symptoms to mitigate possible maternal and fetal adverse outcomes. Future studies with translational approaches (bench to bedside) in prospective large cohorts of pregnant women and using structured interviews to mental diagnosis can favor the identification or corroborate the risk factors associated previously.

## Author statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Journal of Affective Disorders Reports.

## Authors' contribution

H.F.G.B: provided the conception, design of the study, analysis and interpretation of data, drafting the article, revised it critically for important intellectual content, and final approval of the version to be submitted; J.F.G.F: provided the conception, design of the study, analysis and interpretation of data; J.M: acquisition of data, drafting the article, revised it critically for important intellectual content; C.H.P, J.L. P.O, J.P.P.C, C.H.B.M, S.X.P.A, M.A.P.S: acquisition of data; M.A.P.S: revised it critically for important intellectual content, analysis and interpretation of data, drafting the article, and final approval of the version to be submitted.

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## Data statement

The dataset generated and/or analyzed during the current study are not publicly available due on our policy statement of sharing clinical data only request but are available from the corresponding author on reasonable request.

## **Declaration of Competing Interest**

All authors report no conflicts of interest.

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