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Prenatal distress, access to services, and birth outcomes during the COVID-19 pandemic: Findings from a longitudinal study

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ABSTRACT

Background/aims: During the COVID-19 pandemic, pregnant people have experienced disruptions to prenatal care, as well elevated rates of mental health problems and distress. The current longitudinal study aims to understand how different forms of prenatal distress (mental health problems, COVID-19 stressful experiences, and access to prenatal services) impact infant birth outcomes during the pandemic.

Methods: Participants were 265 pregnant individuals from Ontario, Canada. Maternal depression, pregnancy-related anxiety, COVID-related stressors (i.e., financial difficulties, social isolation), and disruptions to prenatal and health services were assessed during pregnancy. Delivery experiences and birth outcomes were assessed in the early postpartum period. Associations between pregnancy stressors and birth outcomes were assessed using path analyses.

Results: Participants reported experiencing substantial changes to their prenatal care due to COVID-19; 23.0 % had prenatal appointments cancelled, 47.9 % had difficulty accessing prenatal classes, and 60.8 % reported changes to their birth plans. Results of path analyses showed a unique effect of pregnancy-related anxiety during the pandemic on lower birth weight, younger gestational age at birth, and more infant birth problems. Further, multi-group path analysis revealed these effects were more pronounced in male infants.

Conclusions: Findings demonstrate that pregnant individuals in Ontario, Canada have experienced considerable disruptions to services during pregnancy. In addition, pregnancy-related anxiety was uniquely linked to elevated risk for adverse birth outcomes, which more heavily impacted male infants. These findings underscore the need for additional mental health support and access to services for pregnant people and their infants, to reduce long-term adverse maternal and fetal health outcomes.

1. Introduction

The COVID-19 pandemic, including nationwide lockdowns, employment changes, and disruption to health-care services, has changed the daily lives of many and resulted in concerningly high levels of distress and mental health problems [1,2]. Pregnant and postpartum women, as well as mothers of young children have been particularly burdened by the pandemic, with documented elevated rates of depression (25–31 %), anxiety (34–42 %) and psychological distress (70 %) [3–5]. During the pandemic, pregnant people have faced distress and

concern for the health and wellbeing of their unborn child [6], unavailability of perinatal medical care, feelings of uncertainty and unpreparedness for birth, and limited social services or access to support [7,8]. A scoping review indicated that reductions in prenatal care visits, the strain on healthcare infrastructure, and early policies to isolate pregnant individuals during labour and delivery have heavily impacted maternal and perinatal health and wellbeing [9]. For example, individuals giving birth during COVID-19 pandemic report lower cognitive functioning compared to those who delivered prior to the pandemic [10]. Although it is well-established that pregnant people are

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experiencing elevated distress and mental health problems during the pandemic [3,4,11], it remains unclear whether mental health problems and COVID-related distress, including disrupted access to care and services, are associated with adverse delivery experiences and birth outcomes. As the pandemic continues into a third year, it is crucial to understand these perinatal effects.

The perinatal period is a time of vulnerability – maternal mental health problems and distress can have detrimental effects on fetal development [12,13]. For example, elevated prenatal distress has been linked to increased risk of miscarriage, reduced gestational age, and lower birthweight [12–14]. Further, in utero exposure to stress can have long-lasting implications for child development, including delays in cognitive and language development [15], alterations in child physiological stress reactivity [16], and elevated risk for obesity [17]. Thus, there is considerable concern that elevated prenatal distress during the COVID-19 pandemic may be linked to adverse birth outcomes and later developmental difficulties.

Inconsistent findings have been reported when comparing the rates of birth outcomes during the pandemic to pre-pandemic periods [18]. For example, some studies have not found a significant difference in the prevalence of preterm births, stillbirths, or lower birth weight during COVID-19 compared to before the pandemic [19,20], others have found that preterm birth was less common during the pandemic compared to before the pandemic [21,22], while others found elevated risk of fetal distress during COVID-19 [23]. To our knowledge, only two longitudinal studies have directly examined the impact of prenatal distress on birth outcomes during the COVID-19 pandemic [24]. Preis et al. (2021) showed that prenatal distress was associated with higher risk for preterm birth and maternal stress was associated with higher risk of small for gestational age in a sample of 1367 women who gave birth in Summer 2020 across the United States [24]. In addition, Giesbrecht et al. (2022) found that fear of COVID-19 during pregnancy was associated with lower infant birthweight and gestational age at birth in a Canadian sample [25]. These studies provide initial evidence that stress during the COVID-19 pandemic is associated with elevated risk of adverse perinatal outcomes. AA additional longitudinal studies have demonstrated the impact of COVID-19 on child developmental outcomes after birth. Provenzi et al. (2021) found that higher levels of prenatal stress (retrospectively reported at birth) were indirectly associated with infant regulatory capacity at age 3 months, in a sample from Northern Italy [26]. In addition, in a not-yet published paper, Deoni et al. found that children born during the pandemic (2020-2021) in the United States, compared to before 2019, had lower cognitive development scores [27]. However, Deoni et al. did not assess the impact of prenatal stress on infant cognitive development. Thus, further research, conducted in countries differentially impacted by the pandemic, is needed to further examine and generalize the longitudinal effects of prenatal stress, mental health and service disruptions, on infant birth outcomes.

The impact of prenatal stress on infant outcomes can differ by fetal sex [27,28]. Sex-specific effects may be related to genetic, epigenetic, or hormonal influences during gestation [29,30]. Greater prenatal stress has been associated with shortened gestational age and increased risk of preterm birth in male, but not female, infants [31]. In addition, higher maternal prenatal cortisol levels were associated with lower infant birth weight and smaller head circumference only among male infants [32]. In contrast, several other studies have found stronger associations between prenatal stress and adverse birth outcomes [33], child brain volume [34], and neuroendocrine functioning (i.e., cortisol levels [16,35]) in females compared to males. Others have failed to find sexspecific effects of prenatal stress on infant birth outcomes [36]. Findings likely vary based on the type of prenatal stress, the child outcome of interest, and the age at which child development was assessed.

1.1. Study Aims

This longitudinal study seeks to examine the unique impact of

varying forms of prenatal stress, occurring during the COVID-19 pandemic, on infant birth outcomes in a Canadian sample. The primary objectives of this study were to: 1) provide descriptive information regarding prenatal care and delivery outcomes; 2) assess the unique impact of prenatal maternal mental health problems, COVID-19 stressful experiences, and access to prenatal care and services, on infant birth outcomes; and 3) examine whether there are sex-specific associations between prenatal stress and infant birth outcomes during the COVID-19 pandemic.

2. Methods

2.1. Participants

A total of 304 pregnant women from Ontario, Canada participated in the first survey (T1) for the COVID-19 and Wellbeing During Pregnancy Study between June and August 2020. Initial recruitment was conducted through social media advertisements, pamphlets distributed to midwifery groups, and word of mouth. At T1, inclusion criteria were that individuals (1) live in Ontario, Canada, (2) read and write English, (3) be at least 18 years of age, and (4) be \leq 36 weeks' gestation. A total of 6 participants withdrew after T1 (4 due to miscarriage, 2 for undisclosed reasons). Participants were also invited to complete surveys each trimester of their pregnancy and during the early postpartum period. Of the remaining 298 eligible participants for follow-up, 265 participants (89 %) completed a postpartum survey between July 2020 and May 2021 (T2). For context, a state of emergency was declared by the provincial government of Ontario three times between March 17, 2020 and April 7, 2021, which included over 300 days of lockdown.

The participants who completed the post-delivery survey did not differ from those who did not complete the survey on parent age, race, ethnicity, education, income, or number of children (ps range 0.10 to 0.80). However, PA participants who entered the study earlier in their pregnancy were less likely to complete the postpartum survey (t(302) = -2.54, p < .05, corresponding to an effect size of r = 0.14).

2.2. Measures

2.2.1. COVID-19 stressful experiences

Participants answered a number of questions regarding the personal impact of the COVID-19 pandemic (see [6,37] for additional details). Some items were dichotomous (yes (1)/no (0)) and others were continuous ranging from 1 (Not at all) to 7 (A lot). A COVID isolation composite was created by summing four dichotomous items related to quarantine, not going to place of work, and not seeing friends or family. A financial difficulties composite was created by averaging six continuous items related to loss of income, reduced job security, and difficulty paying bills and buying groceries.

2.2.2. Centre for epidemiologic studies depression scale (CES-D)

The 10-item CES-D (Anderson et al., 1994) was used to assess the presence of depressive symptoms over the past 7 days. The CES-D total score ranges from 0 to 30; a cut off score of ten or higher indicates the presence of clinically significant depressive symptoms [38]. The CES-D has shown good reliability and validity in pregnant and postpartum samples [39]. The CES-D showed good internal consistency (Cronbach's $\alpha=0.87$) in the current sample.

2.2.3. Cambridge Worry Scale (CWS)

The 16-item CWS [40] was used to assesses pregnancy-specific anxiety (e.g., something being wrong with the baby, possibility of miscarriage, giving birth), as well as general anxiety (e.g., health, money problems, relationship with partner). Participants indicated the degree to which they worry about each item, on a scale of 0 (not a worry) to 5 (major worry). In the current sample, the internal consistency of the CWS was good (Cronbach's $\alpha=0.88$).

2.2.4. Prenatal and delivery outcomes

Participants reported the types of services they had difficulty receiving throughout the duration of their pregnancy, due to COVID-19 restrictions, including prenatal classes, lactation consultation, massage therapy, chiropractic services, and psychological counselling. A cumulative variable was computed by tallying each type of service (possible range = 0–5). Participants also reported whether they experienced complications during pregnancy (e.g., high blood pressure, gestational diabetes, virus or infection). Participants reported on several delivery outcomes, including mode of delivery, infant sex, number of births, gestational age at birth, birth weight, and whether their infants experienced birth problems, including breathing problems/needing oxygen, jaundice, low glucose, NICU treatment, prolonged hospital stay, or malformation. A total score was computed by summing the number of birth problems experienced for each infant (possible range = 0–6).

2.2.5. Sociodemographic and obstetric characteristics

Participants reported sociodemographic characteristics at T1, including maternal age, race, education, income, parity, and gestational age at T1. Throughout pregnancy, participants also reported tobacco use and alcohol consumption.

2.3. Statistical analyses

Descriptive statistics and preliminary correlations were conducted using SPSS 27. Bivariate correlation analyses were conducted to determine relevant covariates (based on prior research) to include in subsequent path analyses. Covariates that had significant bivariate correlations with any of the three infant birth outcomes were controlled for in the path model. Path analyses were conducted in Mplus Version 8 using full information maximum likelihood (FIML) to account for missing data [41] and maximum likelihood ratio (MLR) estimation to derive standard errors. A single path analysis model was derived to simultaneously test the direct paths between prenatal access to care, maternal anxiety and depression, and COVID-19 financial difficulties and social isolation, in relation to infant birthweight, gestational age at birth, and infant birth problems. Given the associations between these birth outcomes, each were correlated with the other. In addition, to assess sex-specific effects, a multi-group path analysis (split by infant sex) was conducted. Model fit was assessed using the comparative fit index (CFI), Tucker-Lewis Index (TLI), root mean squared error of approximation (RMSEA) and Standardized Root Mean Square Residual (SRMR).

3. Results

3.1. Sample characteristics, prenatal care and delivery outcomes

At the onset of the study, participants ranged from 19 to 44 years old (M = 32.02, SD = 4.11 years). Participants were between 4- and 26 weeks gestation (M = 21.93, SD = 8.83 weeks) and 54 % were primiparous. On average, the postpartum survey was completed 48.60 days (SD = 16.44) post-delivery. See Table 1 for additional sample characteristics.

At some point during pregnancy, 91.7 % of the sample was not allowed to bring a support person to their prenatal appointments, 23.0 % had prenatal appointments cancelled, and 73.2 % had prenatal appointments occur by phone or video (3.77 % had cancelled appointments with no virtual visits). In addition, participants reported difficulty accessing services during pregnancy, including prenatal classes (47.9 %). The majority (60.8 %) of the sample also reported experiencing change to their birth plan. Additional details regarding pregnancy and postdelivery experiences are reported in Table 2.

In total, 24.2 % of the sample reported experiencing complications during pregnancy (Table 2). In terms of delivery method, 40.4 % of the sample had a spontaneous vaginal delivery, 28.3 % had an assisted

Table 1
Sample characteristics.

	N (%)/M (SD)
Weeks gestation T1	M = 21.93 (SD = 8.83)
Trimester T1	
First trimester	62 (23.4 %)
Second trimester	116 (43.8 %)
Third trimester	87 (32.8 %)
Number of children	
0	122 (46 %)
1	100 (37.7 %)
2	35 (13.2 %)
≥3	8 (3.1 %)
Marital status	
Married	217 (81.9 %)
Common-law	37 (14.0 %)
In a relationship, but not married or common law	6 (2.3 %)
Divorced	1 (0.4 %)
Separated	1 (0.4 %)
Single	3 (1.1 %)
Race	
White	228 (86.0 %)
Asian	18 (6.8 %)
Indigenous	2 (0.8 %)
Mixed Race	6 (2.3 %)
Other Race	11 (4.2 %)
Education	
Less than high school	1 (0.4 %)
High school	9 (3.4 %)
Non-university postsecondary	69 (26.2 %)
Bachelor's degree	99 (37.5 %)
Above Bachelor's degree	86 (32.6 %)
Annual Family Income	
<\$20,000	3 (1.2 %)
\$20,000 to \$34,999	13 (5.0 %)
\$35,000 to \$69,999	29 (11.2 %)
\$70,000 to \$89,999	36 (14.0 %)
\$90,000 to \$109,999	41 (15.9 %)
\$110,000 to \$149,999	76 (29.5 %)
\$150,000 to \$199,999	39 (15.1 %)
≥200,000	21 (8.1 %)

Note: Gestation at T1, N = 265.

vaginal delivery, 17.7 % had a combination of labour and Cesarean (C)-section, and 13.6 % had a C-section only. In total, 60.2 % of the C-sections were unplanned.

In terms of infant delivery outcomes, 262 women (98.9 %) had a single birth and 3 women (1.1 %) had multiple births (twins). Birth outcomes were assessed for all infants (n = 268). 53 % of (n = 141) infants were male. Infants were born between 28.00 and 42.14 weeks gestation (M = 39.15, SD = 1.90); 7.5 % of the sample were born premature (<37 weeks). Infants weighed between 1.33 and 5.10 kg at birth (M = 3.46, SD = 0.53), 3.7 % were low birth weight (<2.5 kg) and 12.4 % had fetal macrosomia (birthweight >4.0 kg). Mothers reported that 28 % of infants experienced problems during their delivery and 46.6 % experienced at least one problem after birth (e.g., breathing problems, jaundice; see Table 2). A total of 4.5 % of the infants were tested for COVID-19, all were negative for the virus.

3.2. Descriptive results for COVID-19 stress and mental health outcomes

See Table 2 descriptive results for the mental health and COVID-19 experiences scales. In terms of COVID-19 experiences, at the onset of the study (T1), 1.1 % of the sample (n = 3) reported being diagnosed with COVID-19, 43.4 % (n = 115) reported being under self-quarantine, and 71.3 % (n = 189) reported not going to their place of work because of COVID-19. At T1, 57.4 % (n = 152) of the sample scored $\geq \! 10$ on the CES—D, indicating potentially clinically significant levels of depression. There is no established cut off for CWS scores.

Table 2Descriptive statistics: pregnancy experiences, delivery outcomes, COVID-19 stressors and mental health.

	N (%)/ M (SD)
Difficulty accessing services	
Prenatal classes	127 (47.9 %)
Lactation consultation	32 (12.1 %)
Massage therapy	159 (60.0 %)
Chiropractic services	78 (29.4 %)
Psychological counselling	39 (14.7 %)
Changes to birth plan	
Delivery location	35 (13.2 %)
Support people	150 (56.6 %)
Childcare arrangements for other children at home	62 (23.4 %)
Pregnancy complications	
High blood pressure/pre-eclampsia	10 (3.8 %)
Gestational diabetes	22 (8.3 %)
Excessive bleeding	12 (4.5 %)
Accidents/falls	29 (10.9 %)
Bed rest	18 (6.8 %)
Virus or infection	34 (12.8 %)
Miscarriage	1 (0.4 %)
Mode of delivery	
Spontaneous vaginal delivery	107 (40.4 %)
Assisted vaginal delivery	75 (28.3 %)
Combination of labour and C-section	47 (17.7 %)
C-section only	36 (13.6 %)
Maternal problems after delivery	00 (2010 10)
Infection	17 (6.4 %)
Incontinence	37 (14.0 %)
Vaginal tearing	109 (41.1 %)
Excessive vaginal bleeding	17 (6.4 %)
Pain while breathing	1 (0.4 %)
Infant problems after delivery	_ (011.10)
Jaundice	90 (33.6 %)
Low glucose	30 (11.2 %)
Breathing problems/needed oxygen	29 (10.8 %)
NICU treatment	15 (5.6 %)
Prolonged hospital stay	29 (10.8 %)
Malformation	1 (0.4 %)
CES-D T1	M = 11.52 (SD = 6.37)
CWS T1	M = 30.06 (SD = 6.37) M = 30.06 (SD = 6.37)
COVID isolation	M = 3.00 (SD = 0.94)
COVID financial difficulties	M = 3.00 (SD = 0.54) M = 2.38 (SD = 1.40)

3.3. Preliminary bivariate correlations and group comparisons

As shown in Table 3, number of weeks gestation at T1, education, and income were related to different birth outcomes. In addition, males had higher birth weight compared to females. Given the high correlation between education and income (r=0.46, p<.01), only education was retained in subsequent path analyses. Thus, number of weeks gestation at T1, maternal education, and infant sex were included as covariates in the path model.

In addition, there were significant bivariate associations between difficulty accessing services, pregnancy complications, prenatal mental health, and COVID-specific stressful experiences (Table 3). For example, complications during pregnancy were associated with higher levels of prenatal anxiety and depression, as well as lower infant birth weight, gestational age at birth and more infant birth problems. Similarly, difficulty accessing services during pregnancy was significantly associated with higher prenatal anxiety, depression, and COVID-related financial difficulties. At the bivariate level difficulty accessing services and prenatal mental health problems were also associated with more birth problems, but not significantly associated with birth weight or gestational age at birth.

To follow-up these bivariate correlations, we dichotomized the sample to include participants with and without difficulty accessing prenatal care services and conducted an independent samples t-test to assess difference in mental health, COVID-stress and birth outcomes. We found that participants who reported difficulty accessing services endorsed higher prenatal anxiety (t (259) = -3.40, p < .001) and higher

Table 3Preliminary correlations.

	,																	
	T.	7.	.3	4.	5.	.9	7.	8.	.6	10.	11.	12.	13.	14.	15.	16.	17.	18.
1. Weeks gestation T1	ı																	
2. Maternal age	0.03	ı																
3. Race	0.02	0.01	ı															
4. Education	0.02	0.18**	0.14*	1														
5. Income	0.02	0.31	-0.02	0.44**	1													
6. Marital Status	-0.09	0.04	-0.09	-0.19**	-0.13*	1												
7. Infant Sex	0.02	-0.05	-0.08	-0.03	0.01	-0.02	ı											
8. Num. children	0.03	0.29**	-0.07	-0.07	0.01	0.01	-0.08	1										
Preg complications	-0.07	0.01	0.15*	-0.15*	-0.21**	0.01	0.05	-0.05	1									
10. Smoking	0.02	-0.11	-0.05	-0.31**	-0.27**	0.05	0.07	60.0	0.03	ı								
11. Alcohol	-0.09	0.02	-0.05	0.00	0.05	0.10	90.0	-0.04	-0.01	-0.03	ı							
12. Difficulty accessing services	0.15*	-0.10	0.05	-0.11	0.02	-0.01	-0.02	-0.27**	90.0	-0.08	-0.03	ı						
13. Prenatal anxiety	-0.08	0.12	0.16*	-0.19**	-0.17**	0.16*	0.01	-0.16**	0.26**	90.0	-0.05	0.31**	ı					
14. Prenatal depression	-0.03	0.08	90.0	-0.31**	-0.17**	0.13*	0.00	0.08	0.27**	0.09	-0.07	0.27**	0.60	ı				
15. COVID Isolation	0.20*	0.03	0.04	-0.01	0.13*	90.0	0.02	-0.04	-0.01	0.03	-0.04	0.12	0.20**	0.13*	ı			
16. COVID financial	0.02	-0.05	0.15*	-0.23**	-0.28**	0.09	-0.02	-0.10	90.0	0.02	-0.05	0.24**	0.42**	0.29**	0.18**	ı		
17. Birth weight	-0.03	-0.03	-0.10	-0.05	80.0	0.07	-0.13*	0.15*	-0.20**	-0.09	0.01	-0.05	-0.10	0.02	0.01	-0.02	1	
18. Gestational age	-0.10	-0.03	-0.06	-0.05	90.0	0.05	-0.06	0.00	-0.18**	-0.03	0.09	0.00	-0.06	0.01	-0.04	0.02	0.50**	ı
Birth problems	-0.06	-0.02	-0.04	-0.13**	-0.14*	-0.07	-0.12	-0.10	0.26**	0.11	-0.09	0.13*	0.19*	0.18**	-0.04	90.0	-0.31**	-0.38**

Note: Weeks gestation T1 = number of weeks gestation at the onset of the study (T1); race = dichotomous race (White = 0, Non-White = 1); infant sex (male = 1, female = 2); Num. children = number of children (continuous); Preg complications = pregnancy complications (range = 0-4); Smoking = maternal cigarette smoking during pregnancy; Alcohol = maternal alcohol consumption during pregnancy; Gestational age number of weeks gestation at birth; Birth problems = infant problems after birth (range = 0-4). ** p < .05 depressive symptoms (t (263) = -2.67, p < .01). However, participants with and without difficulty accessing prenatal care services did not differ in their reported COVID-19 financial difficulties (t (263) = -1.93, p = .05), social isolation (t (263) = -0.95, p = .34), infant birth weight (t (265) = 1.27, p = .20), gestational age at birth (t (266) = 0.24, p = .81) or birth problems (t (266) = -1.48, p = .14).

3.4. Path model: associations between prenatal experiences and birth outcomes

The path model included prenatal difficulty accessing services, prenatal anxiety and depression, COVID-19 financial difficulties and social isolation, as predictors of infant birth weight, gestational age at birth, and birth problems. As shown in Table 4 and Fig. 1, in the final model, gestational age at T1 remained a significant covariate for gestational age at birth, and infant sex was a significant covariate for infant birth weight and total birth problems (as below). Higher maternal anxiety during pregnancy was significantly associated with lower infant birth weight, younger gestational age at birth, and more infant birth problems. Difficulty accessing services during pregnancy, prenatal depression, and COVID-related isolation and financial difficulties were not significantly associated with any of the birth outcomes.

3.4.1. Sex-specific associations

A multi-group path analysis was conducted to explore sex-specific effects. In terms of infant birth weight, higher prenatal maternal anxiety was significantly associated with lower infant birth weight for male infants ($\beta = -0.230$, SE = 0.101, p = .022) and marginally significant for female infants ($\beta = -0.223$, SE = 0.117, p = .055). In addition, higher maternal depression was associated with higher birth weight for males $(\beta = 0.209, SE = 0.101, p = .027)$ but not females $(\beta = 0.077, SE =$ 0.108, p = .429). Similarly, in male infants only, higher prenatal anxiety was associated with more birth problems ($\beta = 0.224$, SE = 0.105, p =.033; females: $\beta = 0.071$, SE = 0.109, p = .516). In addition, higher levels of isolation were associated with fewer birth problems in male infants ($\beta = -0.207$, SE = 0.097, p = .034), but not associated with birth problems in female infants ($\beta = 0.094$, SE = 0.086, p = .272). Regarding gestational age at birth, despite significant effects in the overall model (Table 4), higher prenatal anxiety was only marginally associated with lower gestational age for male infants ($\beta = -0.196$, SE = 0.112, p =.081) and not associated with gestational age in female infants (β = -0.147, SE = 0.098, p = .135).

4. Discussion

This longitudinal study provides descriptive data regarding the prenatal care disruptions and delivery experiences of pregnant people during the pandemic, as well as evidence of the impact of prenatal

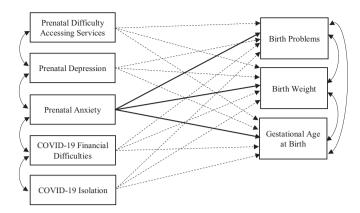


Fig. 1. Path Model: Prenatal experiences in association with infant birth outcomes

Note: Model controls for gestational age at T1, infant sex, maternal education. All predictor variables were intercorrelated, only single correlation arrows are included for a simplified visual depiction. Bolded regression lines indicate significant effects (p < .05), dashed lines are not significant.

psychological distress and COVID-related stressful experiences on infant birth outcomes. Descriptive results demonstrate widespread disruptions to service availability and changes to birth plans. Results from the path analysis (after accounting for the impact of prenatal service disruptions, mental health problems and COVID-specific stressful experiences) indicated that higher levels of maternal anxiety during pregnancy uniquely predicted younger gestational age at birth, lower birth weight, and more parent-reported birth problems. This association remained significant after adjusting for confounders of maternal education, gestational age at T1, and infant sex. In addition, multi-group path analyses revealed sex-specific effects, indicating stronger associations between prenatal distress and birth outcomes for male infants. Taken together, the findings of this longitudinal study highlight the direct impact of the disruptions and distress caused by the COVID-19 pandemic on pregnant individuals and their infants.

The first notable finding is the degree of disruption to social and health services experienced by participants – almost one quarter of the sample (23 %) had prenatal appointments cancelled and 73.2 % switched to telehealth care. Furthermore, nearly half of the sample (47.9 %) reported difficulty accessing prenatal classes as well as other services during pregnancy. These restrictions to social and health services are in response to the Canadian government recommendations for virtual health care appointments, to limit the spread of COVID-19 early in the pandemic [42]. These changes to prenatal care can potentially contribute to elevated uncertainty and distress experienced by pregnant individuals. Notably, the percentage of the current sample who

Table 4Path model regression coefficients.

	Birth weight			Gestational age at birth			Total birth problems		
	В	SE	β	В	SE	β	В	SE	β
Gestational age at T1	-0.003	0.004	-0.043	-0.025	0.013	-0.117*	-0.005	0.006	-0.044
Education	-0.014	0.024	-0.036	-0.066	0.081	-0.049	-0.058	0.043	-0.083
Infant sex	-0.143	0.063	-0.136*	-0.210	0.232	-0.055	-0.226	0.114	-0.116*
Difficulty accessing services	-0.008	0.027	-0.022	0.044	0.074	0.031	0.055	0.045	0.076
Depression (CES-D)	0.011	0.006	0.133	0.020	0.020	0.068	0.009	0.011	0.058
Anxiety (CWS)	-0.007	0.003	-0.211**	-0.020	0.009	-0.159*	0.010	0.005	0.152*
COVID-19 isolation	0.025	0.035	0.045	-0.014	0.114	-0.007	-0.067	0.073	-0.064
COVID financial	0.005	0.022	0.013	0.064	0.080	0.047	-0.030	0.043	-0.043

Note: The model had good fit: CFI = 1.00; TLI = 1.00; RMSEA = 0.00; SRMR = 0.00. Regression coefficients from path model simultaneously including all independent and dependent variables. CES-D = Centre for Epidemiologic Studies Depression Scale, CWS = Centre worry Scale. infant sex (male = 1, female = 2).

^{**} *p* < .01.

^{*} p < .05.

 $[\]hat{p} < .10.$

experienced disruptions to prenatal care corresponds to a nation-wide Canadian sample [43], where, for instance, 40 % experienced cancelled prenatal care appointments. The national study by Groulx et al. [43] also found that disruptions to prenatal care increased the risk of experiencing clinically significant anxiety and depression. Similarly, in the present study we found significant bivariate associations between difficulty accessing services and higher prenatal anxiety and depression. In addition, at the bivariate level, disruptions to services were associated with more birth problems. However, these associations were no longer significant in the path model, after considering maternal mental health and COVID-related stress. Nonetheless, these findings, in combination with prior research, suggest that pregnant Canadians experienced significant disruptions to prenatal care and other health/social services, and that these disruptions were linked to distress.

In terms of delivery and birth outcomes, 68.7% of the sample had a vaginal or assisted vaginal delivery and 31.3% had a C-section (some with partial labour), most of which (60.2%) were unplanned. The rate of C-sections in this sample is only modestly higher than Canada's national rate of 29.1% during 2016–2017 [44]. In addition, the gestational age and rate of premature births (7.5%) in the current sample is comparable to Canadian preterm birth rates from 2019 (8.06%) [45] and Ontario preterm rates between 2006 and 2016 (6.01%) [46]. Only 3.7% of the sample had low (<2.5 kg) birth weight, which is lower than the Canadian (6.5%) and Ontario (6.7%) rates from 2017 [47]. These findings are in line with prior research showing both non-significant differences in preterm birth rates during the pandemic [19,20] and reduced rates of low birthweight infants [48].

Finally, our primary findings indicate that after accounting for difficulty accessing services in pregnancy, prenatal experiences of depression and anxiety, and COVID-19 stressful experiences, pregnancyrelated anxiety emerged as a significant prospective predictor of lower infant birth weight, younger gestational age at birth, and more birth problems. These findings are in line with the large literature showing that prenatal mental health problems are associated with elevated risk to perinatal outcomes [12,14]. We demonstrate that anxiety in pregnancy is uniquely associated with birth outcomes. Our measure of pregnancyrelated anxiety (CWS) included specific concerns related to giving birth, whether partner will be present at birth, and the infant's and mother's health (in addition to broader anxiety, e.g., relationship with partner, financial difficulties). Thus, it is likely that this anxiety measure captured unique distress caused by the pandemic, including health concerns and uncertainty related to birth experiences. In fact, levels of anxiety on the CWS were elevated in the current sample, compared to samples prior to the pandemic [6]. In addition, two prior studies showed that prenatal maternal stress and anxiety [24] and COVID-specific fears [25] were linked to more adverse birth outcomes for births occurring in the summer 2020 in the USA [24]. The current findings build on this prior work by showing that pregnancy-related anxiety early in the pandemic (June-July 2020) predicts birth outcomes spanning from July 2020 to May 2021 in a Canadian sample, after accounting for other forms of pregnancy distress.

In addition, we demonstrated sex-specific associations. Specifically, we found that higher prenatal maternal anxiety was only significantly associated with lower infant birth weight and more birth problems for male infants. We also found that higher maternal depression was associated with heavier birth weight for males only. Perhaps inactivity and changes in appetite, both associated with depression, might contribute to this unexpected finding. Prior research shows similar sex-specific effects, such that prenatal stress was only associated with shortened gestational age and lower birthweight in male infants, but not female infants [29]. Furthermore, recent findings indicate more pronounced effects of the COVID-19 pandemic on cognitive deficits in male infants [27]. In contrast, in the context of natural disasters, prenatal stress has been associated with higher risk for preterm birth and lower birth weight in females, but not males [32]. The chronicity of the COVID-19 pandemic, as compared to most natural disasters, might contribute to

these differing findings. Sex-specific effects may be related to genetic influences, differential placental effects, and fetal sex hormones [29,30,49,50]. Given these inconsistencies, future research is needed to understand how COVID-19 distress is associated with sex-specific birth effects.

There are several potential mechanisms through which prenatal distress can adversely impact birth outcomes. One mechanism involves prenatal exposure to stress hormones, namely cortisol. Although cortisol is essential for fetal growth, excess cortisol exposure can be damaging to fetal development [51]. For example, higher cortisol levels during pregnancy have been associated with lower birth weight [52]. In addition, excessive stress during pregnancy is also associated with dysregulated immune activity, which can adversely impact fetal development [53]. Future research is needed to examine the biological mechanisms linking prenatal distress and infant outcomes during the COVID-19 pandemic.

4.1. Strengths and limitations

This study has several strengths, including the prospective, longitudinal design which spans nearly one year of the COVID-19 pandemic (from June 2020 to May 2021) and permits assessment of prospective associations between prenatal stress and later birth outcomes. However, the current findings must be understood in the context of the study limitations. First, this is a convenience sample who were predominantly low risk in terms of their level of education and income. In addition, mothers who entered the study earlier in their pregnancy were more likely to drop out before the postpartum follow up. Future research is needed to determine the effects of prenatal stress on infant birth outcomes in more diverse samples. Second, data were collected through online questionnaires, therefore birth outcomes were self-reported and not verified by health records. These findings should be validated with future multi-method research that combines self-reported questionnaires and review of health records. Lastly, there are specific pregnancyrelated variables that were not assessed in the current study, such as previous C-sections, fertility treatments and more specific details related to pregnancy complications (e.g., placenta previa), and should be taken into account in future research.

5. Conclusions

This study adds to the voluminous prenatal stress literature by demonstrating the role of prenatal stressful experiences on birth outcomes during the COVID-19 pandemic. Findings demonstrate that pregnant individuals in Ontario, Canada have experienced significant disruptions to social and health services during pregnancy. In addition, pregnancy-related anxiety was uniquely linked to elevated risk for adverse birth outcomes, which more heavily impacted male infants. These findings underscore the need for additional mental health support and access to services for pregnant people and their infants, as they navigate the stressful experiences associated with the COVID-19 pandemic. In addition, this work underscores the need to develop protocols for future public health crises and pandemics [54], to prevent adverse maternal and child outcomes.

Ethical statement

This study was approved by the Hamilton Integrated Research Ethics Board under Project #11034, on June 3, 2020.

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CRediT authorship contribution statement

J.E. Khoury: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Project administration, Writing - Original Draft, Writing - Review & Editing, Funding acquisition; A. Gonzalez: Conceptualization, Methodology, Resources, Project administration, Writing - Review & Editing, Funding acquisition; A. Atkinson Conceptualization, Methodology, Project administration, Writing - Review & Editing; S. Jack: Project administration, Writing - Review & Editing; T. Bennett: Project administration, Writing - Review & Editing.

Declaration of competing interest

The authors do not have any conflicts of interest to disclose.

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References

- J. Bueno-Notivol, P. Gracia-García, B. Olaya, I. Lasheras, R. López-Antón, J. Santabárbara, Prevalence of depression during the COVID-19 outbreak: a metaanalysis of community-based studies, Int. J. Clin. Health Psychol. 21 (1) (2021 Jan 1) 100196
- [2] N. Salari, A. Hosseinian-Far, R. Jalali, A. Vaisi-Raygani, S. Rasoulpoor, M. Mohammadi, S. Rasoulpoor, B. Khaledi-Paveh, Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis, Glob. Health 16 (1) (2020) 1.
- [3] S. Fan, J. Guan, L. Cao, M. Wang, H. Zhao, L. Chen, L. Yan, Psychological effects caused by COVID-19 pandemic on pregnant women: a systematic review with meta-analysis, Asian J. Psychiatr. 1 (56) (2021), 102533.
- [4] H. Yan, Y. Ding, W. Guo, Mental health of pregnant and postpartum women during the coronavirus disease 2019 pandemic: a systematic review and meta-analysis, Front. Psychol. 25 (11) (2020) 3324.
- [5] G. Pariente, O. Wissotzky Broder, E. Sheiner, T. Lanxner Battat, E. Mazor, S. Yaniv Salem, T. Kosef, T. Wainstock, Risk for probable post-partum depression among women during the COVID-19 pandemic, Arch Womens Ment Health 23 (6) (2020) 767–773, https://doi.org/10.1007/s00737-020-01075-3. Epub 2020 Oct 12. PMID: 33047207; PMCID: PMC7549733.
- [6] J.E. Khoury, L. Atkinson, T. Bennett, S.M. Jack, A. Gonzalez, COVID-19 and mental health during pregnancy: the importance of cognitive appraisal and social support, J. Affect. Disord. 1 (282) (2021) 1161–1169.
- [7] C.V. Farewell, J. Jewell, J. Walls, J.A. Leiferman, A mixed-methods pilot study of perinatal risk and resilience during COVID-19, J. Prim. Care Community Health 11 (2020), 2150132720944074.
- [8] S. Meaney, S. Leitao, E.K. Olander, J. Pope, K. Matvienko-Sikar, The impact of COVID-19 on pregnant womens' experiences and perceptions of antenatal maternity care, social support, and stress-reduction strategies, Women Birth 35 (3) (2022) 307–316.
- [9] B. Kotlar, E. Gerson, S. Petrillo, A. Langer, H. Tiemeier, The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review, Reprod. Health 18 (1) (2021) 1–39.
- [10] H. Hamami, E. Sheiner, T. Wainstock, E. Mazor, T. Lanxner Battat, A. Walfisch, T. Kosef, G. Pariente, The association between delivery during the COVID-19 pandemic and immediate postpartum maternal cognitive function, J. Clin. Med. 9 (11) (2020) 3727, https://doi.org/10.3390/jcm9113727. PMID: 33233589; PMCID: PMC7699685.
- [11] S. Sade, E. Sheiner, T. Wainstock, N. Hermon, S. Yaniv Salem, T. Kosef, T. Lanxner Battat, S. Oron, G. Pariente, Risk for depressive symptoms among hospitalized women in high-risk pregnancy units during the COVID-19 pandemic, J. Clin. Med. 9 (8) (2020) 2449, https://doi.org/10.3390/jcm9082449. PMID: 32751804; PMCID: PMC7464613.
- [12] S. Grigoriadis, L. Graves, M. Peer, L. Mamisashvili, G. Tomlinson, S.N. Vigod, C. L. Dennis, M. Steiner, C. Brown, A. Cheung, H. Dawson, Maternal anxiety during pregnancy and the association with adverse perinatal outcomes: systematic review and meta-analysis, J. Clin. Psychiatry 79 (5) (2018 Sep 4) 813.
- [13] S. Madigan, H. Oatley, N. Racine, R.P. Fearon, L. Schumacher, E. Akbari, J. E. Cooke, G.M. Tarabulsy, A meta-analysis of maternal prenatal depression and anxiety on child socioemotional development, J. Am. Acad. Child Adolesc. Psychiatry 57 (9) (2018) 645–657.

- [14] X. Ding, M. Liang, Y. Wu, T. Zhao, G. Qu, J. Zhang, H. Zhang, T. Han, S. Ma, Y. Sun, The impact of prenatal stressful life events on adverse birth outcomes: a systematic review and meta-analysis, J. Affect. Disord. 287 (2021) 406–416.
- [15] S. King, K. Dancause, A.M. Turcotte-Tremblay, F. Veru, D.P. Laplante, Using natural disasters to study the effects of prenatal maternal stress on child health and development, Birth Defects Research Part C: Embryo Today: Reviews. 96 (4) (2012 Dec) 273–288.
- [16] E.Y. Ping, D.P. Laplante, G. Elgbeili, S.L. Jones, A. Brunet, S. King, Disaster-related prenatal maternal stress predicts HPA reactivity and psychopathology in adolescent offspring: project ice storm, Psychoneuroendocrinology 1 (117) (2020), 104607
- [17] K.N. Dancause, D.P. Laplante, C. Oremus, S. Fraser, A. Brunet, S. King, Disaster-related prenatal maternal stress influences birth outcomes: project ice storm, Early Hum. Dev. 87 (12) (2011) 813–820.
- [18] B. Chmielewska, I. Barratt, R. Townsend, E. Kalafat, J. van der Meulen, I. Gurol-Urganci, P. O'Brien, E. Morris, T. Draycott, S. Thangaratinam, K. Le Doare, Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis, Lancet Global Health 9 (6) (2021) e759–e772.
- [19] J. Arnaez, C. Ochoa-Sangrador, S. Caserío, E.P. Gutiérrez, Jiménez M. del Pilar, L. Castañón, M. Benito, A. Peña, N. Hernández, M. Hortelano, S. Schuffelmann, Lack of changes in preterm delivery and stillbirths during COVID-19 lockdown in a European region, Eur. J. Pediatr. 180 (6) (2021) 1997–2002.
- [20] B. Pasternak, M. Neovius, J. Söderling, M. Ahlberg, M. Norman, J.F. Ludvigsson, O. Stephansson, Preterm birth and stillbirth during the COVID-19 pandemic in Sweden: a nationwide cohort study, Ann. Intern. Med. 174 (6) (2021) 873–875.
- [21] V. Berghella, R. Boelig, A. Roman, J. Burd, K. Anderson, Decreased incidence of preterm birth during coronavirus disease 2019 pandemic, Am. J. Obstetr. Gynecol. MFM 2 (4) (2020), 100258.
- [22] G. Hedermann, P.L. Hedley, M. Bækvad-Hansen, H. Hjalgrim, K. Rostgaard, P. Poorisrisak, M. Breindahl, M. Melbye, D.M. Hougaard, M. Christiansen, U. Lausten-Thomsen, Danish premature birth rates during the COVID-19 lockdown, Arch. Dis. Child Fetal Neonatal. Ed 106 (1) (2021) 93–95.
- [23] M. Du, J. Yang, N. Han, M. Liu, J. Liu, Association between the COVID-19 pandemic and the risk for adverse pregnancy outcomes: a cohort study, BMJ Open 11 (2) (2021), e047900.
- [24] H. Preis, B. Mahaffey, S. Pati, C. Heiselman, M. Lobel, Adverse perinatal outcomes predicted by prenatal maternal stress among US women at the COVID-19 pandemic onset, Ann. Behav. Med. 55 (3) (2021) 179–191.
- [25] G.F. Giesbrecht, L. Rojas, S. Patel, V. Kuret, A.L. MacKinnon, L. Tomfohr-Madsen, C. Lebel, Fear of COVID-19, mental health, and pregnancy outcomes in the pregnancy during the COVID-19 pandemic study; fear of COVID-19 and pregnancy outcomes, J. Affect. Disord. 299 (2022) 483–491.
- [26] L. Provenzi, S. Grumi, L. Altieri, G. Bensi, E. Bertazzoli, G. Biasucci, A. Cavallini, L. Decembrino, R. Falcone, A. Freddi, B. Gardella, Prenatal maternal stress during the COVID-19 pandemic and infant regulatory capacity at 3 months: a longitudinal study, Dev. Psychopathol. 2 (2021) 1–9.
- [27] S. Deoni, J. Beauchemin, A. Volpe, V. D'Sa, Impact of the COVID-19 Pandemic on Early Child Cognitive Development: Initial Findings in a Longitudinal Observational Study of Child Health, Medrxiv, 2021.
- [28] S. Sutherland, S.M. Brunwasser, Sex differences in vulnerability to prenatal stress: a review of the recent literature, Curr. Psychiatry Rep. 20 (11) (2018 Nov) 1–2.
- [29] T.L. Bale, Sex differences in prenatal epigenetic programing of stress pathways, Stress 14 (4) (2011) 348–356.
- [30] V. Glover, J. Hill, Sex differences in the programming effects of prenatal stress on psychopathology and stress responses: an evolutionary perspective, Physiol. Behav. 106 (5) (2012) 736–740.
- [31] M.J. Rosa, F. Nentin, M. Bosquet Enlow, M.R. Hacker, N. Pollas, B. Coull, R. J. Wright, Sex-specific associations between prenatal negative life events and birth outcomes, Stress 22 (6) (2019) 647–653.
- [32] A.L. Frith, R.T. Naved, L.A. Persson, E.A. Frongillo, Early prenatal food supplementation ameliorates the negative association of maternal stress with birth size in a randomised trial, Matern. Child Nutr. 11 (4) (2015) 537–549.
- [33] T. Wainstock, I. Shoham-Vardi, S. Glasser, E. Anteby, L. Lerner-Geva, Fetal sex modifies effects of prenatal stress exposure and adverse birth outcomes, Stress 18 (1) (2015) 49–56.
- [34] A. Plamondon, E. Akbari, L. Atkinson, M. Steiner, M.J. Meaney, A.S. Fleming, MAVAN research team, Spatial working memory and attention skills are predicted by maternal stress during pregnancy, Early Human Development. 91 (1) (2015) 23_20
- [35] G.F. Giesbrecht, N. Letourneau, T.S. Campbell, Sexually dimorphic and interactive effects of prenatal maternal cortisol and psychological distress on infant cortisol reactivity, Dev. Psychopathol. 29 (3) (2017) 805–818.
- [36] A.W. Kim, R.S. Mohamed, S. Norris, C. Kuzawa, Maternal Prenatal Stress During the First Trimester and Infant Birthweight in Soweto, South Africa, medRxiv, 2021.
- [37] J.E. Khoury, L. Atkinson, T. Bennett, S.M. Jack, A. Gonzalez, Coping strategies mediate the associations between COVID-19 experiences and mental health outcomes in pregnancy, Arch. Womens Mental Health 19 (2021) 1.
- [38] E.M. Andresen, J.A. Malmgren, W.B. Carter, D.L. Patrick, Screening for depression in well older adults: evaluation of a short form of the CES-D, Am. J. Prev. Med. 10 (2) (1994) 77–84.
- [39] M. Beeghly, K.L. Olson, M.K. Weinberg, S.C. Pierre, N. Downey, E.Z. Tronick, Prevalence, stability, and socio-demographic correlates of depressive symptoms in black mothers during the first 18 months postpartum, Matern. Child Health J. 7 (3) (2003) 157–168.

- [40] H. Statham, J.M. Green, K. Kafetsios, Who worries that something might be wrong with the baby? A prospective study of 1072 pregnant women, Birth 24 (4) (1997) 223 232
- [41] J. Fox, Applied Regression Analysis and Generalized Linear Models, Sage Publications, 2015.
- [42] Canada PHA of, COVID-19: Pregnancy, childbirth and caring for a newborn [Internet], Available from: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/prevention-risks/pregnancy-childbirth-newborn.html, 2021.
- [43] T. Groulx, M. Bagshawe, G. Giesbrecht, L. Tomfohr-Madsen, E. Hetherington, C. A. Lebel, Prenatal care disruptions and associations with maternal mental health during the COVID-19 pandemic, Front. Glob. Womens Health. 23 (2) (2021) 20.
- [44] J. Gu, S. Karmakar-Hore, M.E. Hogan, H.M. Azzam, J.F. Barrett, A. Brown, J. L. Cook, V. Jain, N. Melamed, G.N. Smith, A. Zaltz, Examining cesarean section rates in Canada using the modified Robson classification, J. Obstet. Gynaecol. Can. 42 (6) (2020) 757–765.
- [45] Government of Canada SC, Live births, by weeks of gestation [Internet], Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310042501, 2021.
- [46] J.B. Lee, A. Hinds, M.L. Urquia, Provincial variations in birth outcomes according to maternal country of birth, 2000 to 2016, Health Rep. 31 (4) (2020) 13–21.

- [47] Government of Canada SC, Low birth weight babies, by province and territory [Internet] [cited 2022 Jan 31]. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310040401, 2018.
- [48] S. McDonnell, E. McNamee, S.W. Lindow, M.P. O'Connell, The impact of the Covid-19 pandemic on maternity services: a review of maternal and neonatal outcomes before, during and after the pandemic, Eur. J. Obstetr. Gynecol. Reprod. Biol. 255 (2020) 172–176.
- [49] V.L. Clifton, Sex and the human placenta: mediating differential strategies of fetal growth and survival, Placenta 1 (31) (2010) S33–S39.
- [50] M. Del Giudice, E.S. Barrett, J. Belsky, S. Hartman, M.M. Martel, S. Sangenstedt, C. W. Kuzawa, Individual differences in developmental plasticity: a role for early androgens? Psychoneuroendocrinology 1 (90) (2018 Apr) 165–173.
- [51] R.M. Reynolds, Glucocorticoid excess and the developmental origins of disease: two decades of testing the hypothesis–2012 Curt Richter award winner, Psychoneuroendocrinology 38 (1) (2013) 1.
- [52] M.I. Bolten, H. Wurmser, A. Buske-Kirschbaum, M. Papoušek, K.M. Pirke, D. Hellhammer, Cortisol levels in pregnancy as a psychobiological predictor for birth weight, Arch. Womens Mental Health 14 (1) (2011) 33–41.
- [53] M.E. Coussons-Read, Effects of prenatal stress on pregnancy and human development: mechanisms and pathways, Obstetr. Med. 6 (2) (2013) 52–57.
- [54] M. Konda, B. Dodda, V.M. Konala, S. Naramala, S. Adapa, Potential zoonotic origins of SARS-CoV-2 and insights for preventing future pandemics through one health approach, Cureus. 12 (6) (2020).