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Original data

An emotional distress biomarker in pregnant women: Ultra-short-term heart rate variability

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ABSTRACT

Prenatal emotional distress is common in pregnant women. Altered emotional distress can occur from the very beginning to the end of pregnancy. Heart rate variability (HRV) has recently become considered to be a potentially reliable psychophysiological stress biomarker in adults. In the current study, we evaluated ultra-short-term HRV (1-minute measurement) as a psychophysiological biomarker by examining the association between HRV parameters and self-reported prenatal emotional distress among pregnant women ($N = 230$) across three trimesters of pregnancy.

Results: Prenatal emotional distress was associated with a lower root mean square of successive differences between normal heartbeats (RMSSD), NN50, and SDNN Index among pregnant women who are in the second trimester. For women in the first and third trimester of pregnancy, prenatal emotional distress was not significantly correlated with any HRV indicators.

Limitations: The cross-sectional nature of our results limits the directional expression and assessment of the relationships, and longitudinal studies that target the recruitment of more pregnant women with subtypes of emotional distress issues are also needed.

Conclusions: Time-domain parameters of low HRV (associated with reduced parasympathetic activity) can potentially serve as an efficient psychophysiological biomarker for prenatal emotional distress in the second trimester of pregnancy. However, the time-domain HRV indicators in pregnant women in the first and third trimesters may be affected by other physiological and psychological fluctuations, thus decreasing the HRV biomarker's efficiency in predicting their prenatal emotional distress.

Introduction

Pregnancy brings women into a new life stage that grants them a new name— "mother" —and causes them to experience biological and psychological changes and status transitions both within their family and in society. While some women may perceive pregnancy as a source of satisfaction, self-realization, and maturity, some others may experience emotional distress of different types and degrees and for various reasons—with depression, anxiety, and stress being the most common (Tang et al., 2019; Yuksel et al., 2013). About 10 % of pregnant women worldwide suffer from psychological disorders (who fulfill the diagnostic criteria for depression and anxiety (World Health Organization WHO, 2019).

Using biomarkers along with the psychological assessment tools/scales will help professionals or pregnant women themselves to identify prenatal emotional distress and develop proper interventions to address it. Researchers have developed several instruments exclusively for the pregnant population (e.g., Prenatal Distress Questionnaires (PDQ; Alderdice & Lynn, 2011). In addition to self-report scales, biomarkers such as Heart Rate Variability (HRV) parameters are highly desirable for gauging emotional distress.

HRV, an indicator of ANS activity is considered a promising and increasingly used biomarker for emotional distress (Appelhans & Luecken, 2006; Cattaneo et al., 2021; Castaldo et al., 2015; Hoogwegt et al., 2014).

Accumulated studies investigated the relationship between prenatal emotional distress and HRV parameters during pregnancy (e.g., Brown et al., 2023; Kimmel et al., 2021; Mizuno et al., 2017; Riddle et al., 2023; Rouleau et al., 2016; Shea et al., 2008; Solorzano et al., 2022). For example, a study investigated the role of the rMSSD HRV parameter

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Table 1
Demographic characteristics of the participants (N=230).

Variable	Total Participants (n=230)		Subgroups					
			First Trimester Group (n= 26)		Second Trimester (n = 136)		Third Trimester Group (n = 68)	
	Mean/n	(SD)/ (%)	Mean/n	SD/ (%)	Mean/n	SD/ (%)	Mean/n	SD/ (%)
HRV parameters								
rMSSD (ms)	1.59	(.19)	3.75	(.39)	3.67	(.44)	3.66	(.45)
NN50 (ms)	1.03	(.35)	1.13	(.31)	1.02	(.35)	1.02	(.37)
SDNN (ms)	1.69	(.17)	1.73	(.15)	1.70	(.17)	1.69	(.19)
Prenatal Emotional Distress	4.35	(2.50)	4.92	(2.95)	4.12	(2.42)	4.60	(2.44)
Demographics								
Age (years)	33.42	(3.74)	32.89	(3.67)	33.61	(3.87)	33.24	(3.50)
Pregnancy (weeks)	22.94	(6.78)	11.14	(2.38)	21.30	(3.62)	30.73	(2.74)
Pre-pregnancy weight (kg)	55.66	(11.18)	54.20	(11.07)	56.39	(10.93)	54.76	(11.74)
Current weight (kg)	60.20	(11.71)	55.29	(10.26)	60.47	(10.65)	61.53	(13.77)
Height (cm)	159.87	(5.75)	158.60	(5.53)	160.33	(5.34)	159.44	(6.54)
Current BMI	23.51	(4.04)	21.93	(3.49)	23.50	(3.82)	24.14	(4.52)
Employment								
Full-time	188	(81.74 %)	24	(92.30 %)	111	(81.60 %)	53	(77.90 %)
Part-time	13	(5.65 %)	0	(0.00 %)	10	(7.40 %)	3	(4.40 %)
Housewife	23	(10 %)	1	(3.80 %)	11	(8.10 %)	11	(16.20 %)
Unemployed, Seeking a job	6	(2.61 %)	1	(3.80 %)	4	(2.90 %)	1	(1.50 %)
Education								
Without formal education	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
Primary school	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
Middle high school	2	(0.87 %)	0	(0.00 %)	0	(0.00 %)	2	(2.90 %)
Senior high school	18	(7.83 %)	1	(3.80 %)	9	(6.60 %)	8	(11.80 %)
Diploma	16	(6.96 %)	3	(11.50 %)	10	(7.40 %)	3	(4.40 %)
Bachelor's degree	115	(50 %)	15	(57.70 %)	74	(54.50 %)	26	(38.20 %)
Master's degree	78	(33.91 %)	7	(26.90 %)	42	(30.90 %)	29	(42.60 %)
Doctoral Degree	1	(0.43 %)	0	(0.00 %)	1	(0.70 %)	0	(0.00 %)
Marital Status								
Single	2	(0.87 %)	0	(0.00 %)	0	(0.00 %)	2	(2.90 %)
Married/Cohabitating	228	(99.13 %)	26	(100.00 %)	136	(100.00 %)	66	(97.10 %)
Divorced/Separated	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
Widowed	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
Number of Children								
No children or not applicable	194	(84.35 %)	22	(84.60 %)	116	(85.30 %)	56	(82.40 %)
1 child	33	(14.35 %)	4	(15.40 %)	18	(13.20 %)	11	(16.20 %)
2 children	3	(1.3 %)	0	(0.00 %)	2	(1.50 %)	1	(1.50 %)
3 or more children	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
Income (monthly)								
Not applicable	26	(11.3 %)	3	(11.50 %)	13	(9.60 %)	10	(14.70 %)
Less than 10k HKD	35	(15.22 %)	1	(3.80 %)	19	(14.00 %)	15	(22.10 %)
10–20k HKD	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)	0	(0.00 %)
20–40k HKD	94	(40.87 %)	13	(50.00 %)	54	(39.70 %)	27	(39.70 %)
Above 40k HKD	75	(32.61 %)	9	(34.60 %)	50	(36.80 %)	16	(23.50 %)
History of Mental Health Problems								
No	222	(96.52 %)	24	(92.30 %)	133	(97.80 %)	65	(95.60 %)
Yes	8	(3.48 %)	2	(7.70 %)	3	(2.20 %)	3	(4.40 %)
Chronic illness								
No	215	(93.48 %)	24	(92.30 %)	127	(93.40 %)	64	(94.10 %)
Yes	15	(6.52 %)	2	(7.70 %)	9	(6.60 %)	4	(5.90 %)
Pregnancy Complication								
No	219	(95.22 %)	25	(96.20 %)	130	(95.60 %)	64	(94.10 %)
Yes	11	(4.78 %)	1	(3.80 %)	6	(4.40 %)	4	(5.90 %)

Notes:
* $p < .05$;
** $p < .01$;
*** $p < .001$

using a smartphone application as a predictor of the depression level among Italian pregnant women (N =135; in the second or third trimester) and found that lower prepartum rMSSD was associated with a higher level of depressive symptoms in the postpartum after controlling for other potential covariates (Solorzano et al., 2022). However, considering the limitations of previous studies, such as the equipment's inconvenience (e.g., ECG data, Brown et al., 2023), the small sample size (e.g., Riddle et al., 2022), or the lack of a comprehensive dataset across three pregnancy trimesters (e.g., Kimmel et al., 2021; Shea et al., 2008; Solorzano et al., 2022), it is essential to further explore such topic. In order to fill in the research gap, in this study, via using a cross-sectional dataset (N = 230), we aimed to examine the relationship between prenatal maternal emotional distress and ultra-short-term (60 s) HRV parameters among women in three trimesters of pregnancy. The HRV parameters were examined by a well validated and portable equipment—*Elite HRV* with Corsense Monitor (Perrotta et al., 2017).

Prenatal Maternal Emotional and Physiological Distress

Pregnancy-specific emotional distress refers to a spectrum of psychological concerns during pregnancy, baby delivery, and the postnatal period. Such concerns include but not limited to daily worries, limited psychosocial harmony, depression and anxiety (Alderfice & Lynn, 2011). Pregnant women experience emotional distress originating from

Table 2
Subgroup linear regression predicting heart rate variability parameter: rMSSD by prenatal emotional distress.

		First Trimester		Second Trimester		Third Trimester	
		β	*p*	*β*	*p*	*β*	*p*
Level 1	Age	−.64*	.030	−.20*	.028	−.23	.095
	Current BMI	−.19	.344	−.09	.336	−.01	.938
	Number of Children	.45	.135	−.22*	.015	.22	.117
	Income	−.03	.927	−.15	.194	.002	.990
	Employment Status	.17	.625	−.08	.478	.13	.454
	Mental Health Problems	.18	.537	.07	.402	−.04	.743
Level 2	Prenatal Emotional Distress	−.16	.528	−.19*	.025	−.09	.536
Model Summary	First Level's R^2	.334		.106		.077	
	Second Level's R^2	.349		.141		.083	
	R^2 change	.015		.034		.006	
	F in level 1	$F = 1.59$, $p = .204$		$F = 2.56$*, $p = .022$		$F = .85$, $p = .540$	
	F in level 2	$F = 1.38$, $p = .272$		$F = 3.00$*, $p = .006$		$F = .77$, $p = .612$	

Notes:
† $p < .06$;
* $p < .05$;
** $p < .01$;
*** $p < .001$.

Table 3
Subgroup linear regression predicting heart rate variability parameter: NN50 by prenatal emotional distress.

		First Trimester		Second Trimester		Third Trimester	
		β	*p*	*β*	*p*	*β*	*p*
Level 1	Age	−.50	.100	−.13	.153	−.20	.149
	Current BMI	−.40	.075	−.11	.224	−.10	.436
	Number of Children	.37	.238	−.18*	.045	.20	.153
	Income	.22	.562	.02	.899	.08	.650
	Employment Status	−.13	.707	−.15	.207	.08	.654
	Mental Health Problems	.18	.560	.07	.415	−.02	.860
Level 2	Prenatal Emotional Distress	−.21	.455	−.18*	.038	−.02	.897
Model Summary	First Level's R^2	.244		.068		.083	
	Second Level's R^2	.268		.099		.083	
	R^2 change	.024		.031		.000	
	F in level 1	$F = 1.02$, $p = .440$		$F = 1.58$, $p = .158$		$F = .92$, $p = .489$	
	F in level 2	$F = .94$, $p = .500$		$F = 2.12^{\dagger}$, $p = .051$		$F = .78$, $p = .610$	

Notes:
† $p < .06$;
* $p < .05$;
** $p < .01$;
*** $p < .001$.

various issues, including physical symptoms and changes, physiological, emotional, and interpersonal changes, bodily changes, concerns about parenthood, and worries about labor, delivery, and the baby's development (Yuksel et al., 2013). Depression, stress, and anxiety are the most commonly associated to maternal emotional distress which are highly prevalent among pregnant women. Prenatal stress, anxiety, and depression have been reported by several international studies to be, respectively, 12–84 %, 18.2–29.6 %, and 7.4–12.8 % (Bennett et al., 2004; Dennis et al., 2017; McDonald et al., 2013; Wu et al., 2021). In China, a national survey among women in early pregnancy in Chongqing revealed the prevalence of stress, anxiety, and depression in pregnancy at 91.86 %, 15 %, and 5.19 %, respectively (Tang et al., 2019).

During pregnancy, the activity of the autonomic nervous system (ANS) varies greatly and adapts to the new requests of the developing fetus (Solorzano et al., 2022). Successful pregnancies are characterized by substantial, adaptive ANS, which are hypothesized to serve a protective function for both the mother and the fetus. In contrast, a large body of research indicates the fact that prenatal maternal emotional distress is linked to maladaptive ANS that may lead to adverse pregnancy outcomes, such as cognitive dysfunctions, cardiovascular diseases, and adverse postnatal mental health outcomes in women(e.g., gestational hypertension), and adverse fetal outcomes such as neurodevelopmental disorders (Challacombe et al., 2023; Christian, 2012; Kim et al., 2018; Manzari et al., 2019). Given that the maladaptive ANS is associated with prenatal emotional distress, it is critical to assess ANS in a reliable and valid manner (e.g., Heart Rate Variability, HRV) in order to facilitate rigorous research and inform efficient intervention.

Prenatal Emotional Distress and Heart Rate Variability (HRV)

A growing body of research has demonstrated that lower HRV is associated with various forms of emotional distress among non-pregnant adults (Appelhans & Luecken, 2006; Cattaneo et al., 2021; Castaldo et al., 2015; Hoogwegt et al., 2014). In the short term, an increase in heart rate reflects an adaptive response to emotional distress, allowing a quick reaction to perceived threat. However, persistent lower HRV (i.e., autonomic imbalance) can lead to excessive destruction on physiological systems and can contribute to increasingly risk of cardiac related issues (Rouleau et al., 2016).

Emerging evidence regarding the significant association between prenatal emotional distress issues and reduced heart rate variability parameters over the course of gestation have been reported among pregnant women (Brown et al., 2021; Christian, 2012; Mizuno et al., 2017; Shea et al., 2008; Solorzano, 2022). For example, in a study with 135 pregnant women during their second or third trimester, results revealed that lower prepartum HRV parameters (e.g., rMSSD) predicted

Table 4
Subgroup linear regression predicting heart rate variability parameter: SDNN by prenatal emotional distress.

		First Trimester		Second Trimester		Third Trimester	
		β	p	β	p	β	p
Level 1	Age	−.73*	.015	−.23*	.011	−.13	.353
	Current BMI	−.24	.243	.02	.862	−.14	.281
	Number of Children	.45	.133	−.17	.064	.15	.290
	Income	.30	.401	−.09	.437	−.05	.772
	Employment Status	−.12	.724	−.04	.738	.14	.413
	Mental Health Problems	.26	.377	.05	.566	−.08	.552
Level 2	Prenatal Emotional Distress	−.32	.227	−.20*	.022	.12	.394
Model Summary	First Level's R^2	.301		.065		.098	
	Second Level's R^2	.356		.103		.109	
	R^2 change	.056		.038		.011	
	F in level 1	$F = 1.36$, $p = .280$		$F = 1.49$, $p = .186$		$F = 1.10$, $p = .371$	
	F in level 2	$F = 1.42$, $p = .256$		$F = 2.09$*, $p = .049$		$F = 1.05$, $p = .408$	

Notes:
† $p < .06$;
* $p < .05$;
** $p < .01$;
*** $p < .001$.

higher depressive symptoms in the postpartum (Solorzano et al., 2022). One study conducted among 81 pregnant women during the late second and early third trimester (range: 25–31 weeks; $M = 27.2$ weeks) found that depressed pregnant women had significantly reduced time-domain HRV parameters (e.g., SDNN) while asleep, compared to non-depressed pregnant women (Shea et al., 2008). These findings suggested that prenatal emotional distress may be associated with lower maternal HRV parameters, especially in the time-domain. However, the knowledge of how HRV related to emotional distress across different trimester of pregnancy remained limited. (*for more information about HRV parameters, please read the supplemental document S1*).

Changes of Prenatal Emotional Distress and Heart Rate Variability (HRV) across Three Trimester of Pregnancy

Regarding the variation of emotional status across the pregnancy trimesters, evidence from previous research is mixed. Some researchers suggested that level of emotional distress fluctuated substantially over the course of pregnancy (e.g., Caparros-Gonzalez et al., 2017; Ibrahim & Lobel, 2020; Okagbue et al., 2019; Romero-Gonzalez et al., 2018). For example, in a systematic review analyzed 26 articles relevant to depressive conditions in pregnancy and trimesters revealed that antepartum depression occurs the most frequently in the last trimester of pregnancy and the least in the second trimester (Okagbue et al., 2019). In addition, Romero-Gonzalez et al. (2018) found a u-shaped pattern that emotional distress decreased from the first to the second trimester but rebounded during later pregnancy. While some researchers revealed that no evident change in proportion of women who reported problems with emotional distress issues across different pregnant stages (e.g., Wu et al., 2021). For example, in Wu et al. (2021)'s study with 908 pregnant women in Guangzhou, China, the results revealed that pregnant women who reported having problems with anxiety/depression remained relatively constant throughout the duration of pregnancy, which reflected that prenatal emotional distress may not be affected by their gestational stages.

Previous studies reported a normative increase in parasympathetic nervous system (PNS) and decrease in sympathetic nervous system during the first trimester of pregnancy; however, the second and the third trimester is characterized by an increase in SNS activity and a decrease in PNS activity (SNS) (e.g., Alam et al., 2018; Kuo et al., 2000; Sarhaddi et al., 2022). For example, in Alam et al. (2018)'s study, they argued that NN50 and pNN50 increased significantly in the first trimester of the pregnancy group when compared with non-pregnant control groups. It has also been suggested that there is increased sympathetic activity and decreased parasympathetic activity that characterize autonomic nervous system activity in normal pregnancy irrespective of trimester (e.g., Solanki et al., 2020). In other words, there seems no significant pattern change of HRV across three trimesters. Notably, Solanki and colleagues (2020) suggest that the mostly decline of HRV happen during the second trimester.

Hence, regarding the mixed findings of the HRV parameters and its relation to emotional distress across the pregnancy stages, it is critical to further examine HRV parameters and prenatal emotional distress in pregnant women with respect to pregnancy trimester and see whether and how HRV relates to emotional distress in different pregnancy trimester. To our best knowledge, our study will be the pioneer study to investigate such topic across three trimesters of pregnancy.

Ultra Short Term HRV Equipment—Elite HRV

Traditionally, raw HRV data are collected using an echocardiogram (ECG) reflected in mathematic calculations by hand or with software (Seltzer et al., 2021). Recently, emerging products have been commercialized to streamline this process without a traditional ECG and have been shown to effectively capture variations in HRV (Dostal et al., 2019; Ng et al., 2022; Schlicht et al., 2018; Schumann et al., 2021; Seltzer et al., 2021). It has been argued that HRV parameters by the classic ECG and mobile technology derived approaches are not equivalent, such as that portable devices may demonstrate a small amount of absolute error due to few artefacts (e.g., hand movements) when compared to traditional ECG (Guzik et al., 2018). Nevertheless, considering its improved practicality and compliance in the field setting, a recent meta-analysis showed that the small error is in an acceptable range (Dobbs et al., 2019).

For this study, we used the *CorSense* monitor, a one-lead portable ECG that clips onto the participant's index finger (Perrotta et al., 2017). The *CorSense* monitor can be paired to *Elite HRV*, a simple-to-use smartphone app available for iOS and Android devices (Himariotis et al., 2022). The *Elite HRV* calculates the HRV score on a rolling 15-second basis during the reading (Perrotta et al., 2017). Obvious artifacts are cleaned. The artifact detection algorithm is proprietary and data recordings adhere to the industry-standard formulas (Himariotis et al., 2022). The *Elite HRV*'s validity has been revealed to be comparable to traditional HRV software such as *Kubios* for calculating resting time-domain HRV parameters (e.g., rMSSD) (Himariotis et al., 2022; Perrota et al., 2017; Vondrasek et al., 2023). For example, Himariotis et al. (2022) compared the data quality and validity of lnRMSSD between *Elite HRV* data analytic system and an independent criterion—*Kubios HRV* 3.5.0 software. The results showed no significant difference in the lnRMSSD data identification between these two calculation systems (i.e., *Elite HRV* versus *Kubios 3.5.0*). In addition, excellent agreements (ICC =.938–.998) and very strong relations (r =.889–997) were obtained throughout all correction levels (Himariotis et al., 2022). The *Elite HRV* is reasonably inexpensive and compiles HRV data metrics within the program (Dostal et al., 2019). External software processing is no longer required. The monitor and application are portable, allowing for assessment outside a medical facility (Himariotis et al., 2022). Unlike a standard ECG, it does not offer a raw rhythm strip, which is convenient and practical for our participants—pregnant women.

It has been recommended that shorter measurement durations (1–5 mins) are desirable for daily HRV monitoring in order to enhance convenience and increase its utilization in field setting (Castaldo et al., 2019). Although currently 5-mins recording are regarded as being an appropriate option for HRV measurement to detect mental health problems, considering the practical feasibility of wearing portable devices, emerging research paid attention to the applicability of using duration shorter than 5 min (e.g., 60 s) (Esco & Flatt, 2014; Castaldo et al., 2019). Several studies compared different time durations (ranges from 1 to 5 mins) and proved that 60 s appears to be an acceptable recording time for time-domain HRV parameters among healthy subjects by using ECG (Esco & Flatt, 2014), the *Elite HRV* device (Moya-Ramon et al., 2022) and other portable devices (Chen et al., 2020).

In the current study, we utilized the ultra-short-term (60 s) HRV measurement, providing the user with a 60 s-readout after a session is completed (Dostal et al., 2019; Moya-Ramon et al., 2022; Shaffer et al., 2016; Shaffer & Ginsberg, 2017). Time-domain (e.g., rMSSD, SDNN, NN50) and frequency-domain indices (e.g., HF, LF, LF/HF ratio) and geometric measures are two domains for collecting standard HRV parameters. For short-term HRV data collection (1–5 mins), while the conventional short-term recording standard is 5 min, recent studies have also supported the validity of 60 s recording time of time-domain parameters such as rMSSD, SDNN, NN50 (Chen et al., 2020; Shaffer & Ginsberg, 2017). The Elite HRV system applies the 60 s HRV time-domain parameters calculation (e.g., rMSSD, SDNN, NN50) via industry standard (Seltzer et al., 2021; Perrotta et al., 2017). However, for frequency-domain parameters, no prior studies have validated the validity and reliability of the 60 s period recording frequency-domain parameters. Some researchers argue that the minimum recording time for frequency-domain parameters should be more than 3 mins for HF (Chen et al., 2020) and 2 mins for LF (Shaffer et al., 2014). Therefore, in the current study, we collected 60 s recordings of three validated and reliable time-domain parameters (i.e., rMSSD, SDNN, NN50).

The Present Study

Studies of HRV in pregnancy should significantly enhance our knowledge of the effects of emotional distress. Since the autonomic dysregulation may present well before the manifestation of the clinical symptoms, such information could provide as a useful prognostic indicator of risk. In current study, we aimed to explore the relationship between HRV parameters and prenatal emotional distress across three trimesters of pregnancy by using the ultra-short-term 60 s HRV equipment. Specifically, the present study hypothesized that ultra-short-term HRV parameters (1-minute measurements) could serve as a prenatal maternal emotional distress indicator in pregnant women. We hypothesized that low HRV-parameter values would be associated with high values for prenatal emotional distress. Due to the lack of evidence regarding the different pattern of HRV parameters and emotional distress across trimester of pregnancy, we did not set a specific hypothesis on subgroup differences.

Methods

The Study Sample

The participants were pregnant women who were recruited from the public through advertising via social media (Facebook, WhatsApp), promotional emails, and posters/brochures at maternity clinics. Perinatal women applicants who were interested in the program were prescreened for eligibility by our research associates via online application questionnaires. Those who met the primal inclusion criteria were further contacted for a 10- to 15-minute intake video screening using a one-to-one interview by a licensed professional, to verify each applicant's eligibility. Specifically, the clinical professional asked the applicants whether they have a history of mental health problems (e.g., depression, anxiety, and stress), chronic illness (e.g., pain syndrome) and pregnancy complications (e.g., high blood pressure, gestational diabetes; persistent nausea). The inclusion criteria were that participants 1) be age 18 years old or above, 2) understand Chinese (reading and speaking), 3) had been pregnant for less than 30 weeks, 4) were without serious pregnancy complications (e.g., a placental abnormality, multiple gestations, preterm labor, or required bed rest), 5) had no high-risk psychiatric conditions (e.g., schizoaffective disorder, bipolar disorder, or current psychosis; imminent suicide or homicide risk), and 6) currently had no cardiovascular diseases. Ethical approval was obtained from the ethical review board of the XXX university (with the No. XXX). All participants provided informed consent to participate in this research.

A prior power analysis (GPower, version 3.1) was conducted, by expecting a 90 % power with a type I error of 5 %, suggesting a minimal sample size of 24 based on a linear regression model of seven predictors and one tested predictor with an effect-size of.60 (Faul et al., 2009). Previous research also suggested that the minimum sample size should be 25 for regression (Jenkins, Quintana-Ascencio, 2020).

Four hundred and seventy-seven potential participants expressed interest in the program by submitting an electronic application form. Subsequently, 315 of the applicants attended a 15-minute one-to-one Zoom screening interview conducted by senior research assistants. The interview served three purposes: 1) examine the eligibility of the participants, 2) introducing the program in detail and addressing concerns, and 3) seeking informed consent. Ultimately, 245 participants signed and submitted the consent form via email. The recruitment was conducted between May 2021 and October 2022.

A mobile device for monitoring HRV—a *CorSense* monitor (Perrotta et al., 2017; Moya-Ramon et al., 2022) —was mailed to each participant, who was invited to continuously measure HRV for seven days (for 60 s per day, during the morning time). After starting the HRV measurement, each participant was asked to fill out an online questionnaire via Qualtrics. Ultimately, 235 participants completed the seven-day HRV measurements, and 232 submitted the questionnaire. After we matched the HRV and questionnaire data, the data set comprised 230 cases.

Study Design and Protocol

The study was cross-sectional and was performed in a single session with each participant. For the pregnant women who agreed to participate, a researcher described the study, and a consent form was provided to eligible applicants. The participants were then asked to complete questionnaires to report their demographic information and their prenatal emotional distress.

In addition, the participants were asked to record their HRV data using the *CorSense* monitor paired with the mobile App *Elite HRV* (Perrotta et al., 2017; Moya-Ramon et al., 2022). Participants were asked to find a comfortable position with their eyes closed, and to place the CorSense monitor on the index finger of their choice. The monitor recorded a 60 s, at-rest reading. To guarantee the rigor of the HRV data, we asked participants to complete the 1-minute reading no later than 12:00 PM per day for seven continuous days. No additional instruction was provided for the respiratory pattern during the recording sessions.

Measures

Heart Rate Variability Parameters

The HRV parameters are summarized in Table 1. Time-domain analyses of recording data involve simple calculations of mean normal-to-normal (NN) intervals and the variance between NN intervals (Malik, 1996). One frequently used time-domain analysis index of physiological resilience against stress is the standard deviation of the NN interval (SDNN). When HRV is large and irregular, the SDNN value increases. We also measured the following additional parameters: the root mean square of the successive differences (RMSSD), and the number of interval differences of successive NN intervals greater than 50 (NN50). The parasympathetic nervous system impacts these variables. In total, we used three time-domain HRV parameters in this study to test the association between HRV and psychological stress: the RMSSD, NN50 and SDNN.

Prenatal Emotional Distress

Via our questionnaire, the subscale of the Prenatal Distress Questionnaire (PDQ)—prenatal emotional distress (three items)—was utilized to measure the participants' pregnancy-emotion-specific level of distress (Chan, 2015; Yali & Lobel, 1999). Responses were submitted via a 5-point Likert scale ranging from 0 (*not at all*) to 4 (*extremely*). Responses to the three items were summed, providing a prenatal emotional distress score ranging from 0 to 15. A sample item was "Emotional ups and downs during pregnancy annoy me." In this study, the Cronbach's alpha was 0.73.

Analytic Methods

This study employed IBM SPSS (version 26) software for data analysis. We used the mean of seven-days HRV parameters in the data analysis. Due to the skewness of the HRV parameters, log-transformation was applied to the rMSSD, NN50, and SDNN (Solorzano et al., 2022). One-way ANOVAs were used to determine whether or not there is a statistically significant difference of study variables between the means of three trimester groups. Linear regressions were conducted to test the relationships between the HRV parameters (rMSSD, NN50, and SDNN) and emotional distress. The significance level was set to $p < .05$. Standardized regression coefficients (beta coefficients or beta weights) were obtained. Six demographic variables were controlled for and used as independent variables at the level 1 in regression test (age, current BMI, number of children, income and employment status, and history of mental health problems). Prenatal emotional distress was the independent variable in the linear regressions in level 2 in regression test. The HRV parameters (rMSSD, NN50, and SDNN) were listed as dependent variables, respectively. Participants were divided into three groups according to their pregnancy weeks: first trimester (less than 14 pregnancy weeks), second trimester (14–28 pregnancy weeks), third trimester (more than 28 pregnancy weeks). Linear regressions were conducted in three groups respectively.

Results

Sample Characteristics

Table 1 summarizes the demographic characteristics of the participants. There were 230 participants in total, with a mean age of 33.42 years ($SD = 3.74$), a mean pre-pregnancy weight of 55.66 kg (SD = 11.18), and a mean height of 159.87 cm (SD = 5.75). Their mean week of pregnancy was 22.94 weeks (SD = 6.78). They had a mean current weight of 60.20 kg (SD = 11.71) and a mean current BMI of 23.51 (SD = 4.04). Of the participating pregnant women, most were employed in full-time positions (81.74 %), a few were employed part-time (5.65 %), and homemakers were the second-largest employed group (10 %). Most were married or living with their partners (99.13 %), and most had no children (84.35 %). Most of them had an educational level of a university degree or above (83.91 %). The lowest level of education for the participants was middle high school (0.87 %), with only two in that category of having finished only middle high school. The largest group of participants had a monthly income range between 20k and 40k Hong Kong dollars (HKD), followed by those with a monthly income above 40k (32.61 %), and with much smaller groups below 10 HKD or not applicable. Regarding health conditions, only 6.52 % of the participants reported having a chronic illness, 4.78 % had pregnancy complications, and 3.48 % had a history of mental disorders.

Table 1 presents pregnancy emotional distress and HRV parameters in three subgroups. One-way ANOVAs were performed to compare the effect of pregnancy trimesters on prenatal emotional distress and HRV parameters (i.e., rMSSD, SDNN, NN50). Results showed no significant group difference in pregnancy emotional distress ($F = 1.631$, $p = .198$), rMSSD ($F = .369$, $p = .692$), SDNN ($F = .395$, $p = .674$), and NN50 ($F = 1.043$, $p = .354$).

Linear Regressions Predicting Prenatal Emotional Distress by HRV Parameters

As shown in Tables 2–4, HRV parameters were tested respectively for associations with prenatal emotional distress in three trimester subgroups. Specifically, in the first trimester and third trimester subgroups, prenatal emotional distress was not associated with HRV parameters. In the second trimester subgroups, prenatal emotional distress was significantly associated with HRV parameters reflected by lower rMSSD ($\beta = -.015$, $p = .025$), NN50 ($\beta = -.026$, $p = .038$), and SDNN ($\beta = -.014$, $p = .022$).

Discussion

Our results revealed that, only for pregnant women in the second pregnancy trimester, the association between HRV parameters (RMSSD, NN50, and SDNN) with prenatal emotional distress was significant. For the pregnant women who are in the first and third trimester of pregnancy, there is no evident results regarding the relationship between HRV parameters and prenatal emotional distress.

Low parasympathetic activity, and possibly also high sympathetic activity, were related to higher reports of certain forms of emotional distress for women during second trimester pregnancy: specifically, it may reflect a pattern of sympathetic activity being dominant over parasympathetic activity. Because a reduction of HRV (e.g., reduced parasympathetic activity with or without increased sympathetic activity) is a known pathway to increase morbidity and mortality, HRV may serve as a biomarker linking prenatal emotional distress to illness and adverse outcomes. Those results are aligned with abundant previous studies conducted with pregnant women (Brown et al., 2023; Kimmel et al., 2021; Mizuno et al., 2017; Riddle et al., 2023; Rouleau et al., 2016; Shea et al., 2008; Solorzano et al., 22).

Interestingly, our findings suggest the different patterns of relationship between HRV parameters and prenatal emotional distress across different pregnancy trimesters. In our research, the only significant association between HRV parameters and emotional distress was found among the women in the second trimester but not the first and the third trimester. Our findings indicate that, compared with pregnancy during the first and third trimesters, both HRV parameters and emotional distress fluctuate less in the second trimester of pregnancy, which could be a relatively stable period for efficient and rigorous assessment of the relationship between HRV and emotional distress.

To the best of our knowledge, no study has yet investigated how the relationship between HRV and emotional distress changes with the increasing of gestational stage. One possible explanation for these findings is that, compared with middle pregnancy, both early and late pregnancy are associated with more significant physiological and psychological challenges, which may disturb the relationship between HRV and perinatal emotional distress. Previous research related to physiological and psychological change across pregnancy may provide supportive arguments (Ibrahim & Lobel, 2020; Wu et al., 2021). Pregnant women during the first trimester may experience a high fluctuation in physiological (e.g. morning sickness, severe vomiting, and fetal loss risk; Wu et al., 2021) and psychological experiences (Braeken et al., (2015). At later stages of pregnancy, problems arise with mobility, self-care, and daily activity due to the progressive distension of the belly and the associated inconvenience (Setse et al., 2009). In addition, some pregnant women in the third trimester experience additional physical discomfort, such as pelvic pain and chest distress, as a direct result of the enlargement of the uterus (Wu et al., 2021). Moreover, psychological complications, fear of childbirth, and the impact of pregnancy on sexual life may elevate their unstable health status in the third trimester (Bjelica et al., 2018). In contrast, compared with the first and the third trimester, the second trimester is usually a happy time for pregnant women (Türk et al., 2017). During the second trimester of pregnancy, due to a decrease in levels of human chorionic gonadotropin hormone and an adjustment to the levels of estrogen and progesterone hormones, morning sickness usually lessens, and extreme tiredness and breast tenderness usually ease up (Wu et al., 2021). For example, in Wu et al. (2021) study about health status across three trimesters of pregnancy, both the physiological and psycho-behavioral levels of pregnant women were the highest in the second trimester. Therefore, the relatively difficult time and physiological challenges in the first trimester and the third trimester might be a possible reason why the association between HRV parameters and emotional distress is masked and becomes less clear.

To summarize, overall, our results suggest that low HRV (indicated by time-domain parameters) during the second trimester of pregnancy could serve as an efficient biomarker for prenatal emotional distress by reflecting prenatal-stress-induced changes in the autonomic nervous system. It was also revealed that time-domain HRV parameters could be an efficient biomarker for emotional distress for pregnant women in the second trimester (Brown et al., 2023; Kimmel et al., 2021; Mizuno et al., 2017; Riddle et al., 2023; Rouleau et al., 2016; Shea et al., 2008; Solorzano et al., 22). For pregnant women in the first and third trimester, however, researchers should interpret the assessment of HRV and its effect on predicting emotional related issues in a more cautious way.

Strengths, Limitations, and Future Directions

Given our findings of the associations between HRV parameters and prenatal emotional distress, ultra-short-term (1-minute) HRV could be used as an efficient and objective tool to assess emotional distress during the second trimester of pregnancy.

One strength of this study is that we contribute to the scarce literature linking HRV and maternal emotional distress during pregnancy. Specifically, the essential strengths of this study are (1) the rigorous HRV measurements, with several calculated parameters, (2) the repeated HRV measures for seven continuous days, thus guaranteeing the data's rigor, and (3) the exploration of subgroup analyses across three trimesters of pregnancy.

Concerning the self-report questionnaires, we need to consider that overreporting or underreporting is possible and that a broad definition of emotional distress was used. A further criticism is that we could not check whether the self-report data reflected persistent distress, because no further validated questions on chronicity were included. These problems with the self-reporting of emotions and with events questionnaires may impede links between questionnaire results and biological information such as HRV. Given the complexity of prenatal emotional distress, a multi-approach diagnosis conducted both pre-pregnancy and during pregnancy may be necessary. Moreover, because of the physiologic changes during pregnancy, these women had a naturally occurring increase of sympathetic input. Future research should consider the influence of specific physiologic problems on the relationship between psychological stress and HRV, through systematic assessments (e.g., of gestational diabetes, gestational hypertension, insomnia, and hypersomnia).

Second, the cross-sectional nature of our results limits the directional expression and assessment of the relationships, and longitudinal studies that target a recruitment of more pregnant women with subtypes of emotional distress issues (e.g., depression, anxiety, and stress subgroups) are also needed. More extensive longitudinal studies would allow investigations of changes and the interconnections between HRV and emotional distress in each individual, across the prenatal period. More extensive longitudinal studies would also improve our understanding of HRV as a helpful biomarker for predicting emotional distress during pregnancy. Longitudinal studies of pregnant women's HRV and psychological stress would allow us to compare changes both between individuals and within individuals, in an effort to assess the changing balance in autonomic nervous system functioning. Moreover, longitudinal studies would allow us to understand the late-pregnancy associations between HRV parameters and emotional distress in both maternal and child outcomes.

Third, since other potentially useful frequency-domain HRV parameters did not show acceptable reliability under the 60 s duration HRV recording (e.g., LF), we considered only three time-domain HRV parameters, which preclude the possibility of confirming HRV's applicability as an efficient biomarker of prenatal emotional distress in a more complete framework.

Fourth, previous studies showed good validity of mobile HRV measurement under the ultra-short-term recording duration when compared to traditional ECG devices among the general population (Chen et al., 2020; Esco & Flatt, 2014; Moya-Ramon et al., 2022) but not among pregnancy sample in particular. Future studies comparing data from the traditional ECG with HRV mobile devices in prenatal settings are warranted (e.g., measuring 1-minute HRV multiple times to estimate the test-retest reliability).

Fifth, future studies of HRV measurement during pregnancy should establish a range of normal HRV values, and such standardization will require the inclusion of both pregnant and non-pregnant women. Finally, normal values for HRV measures may need to be adjusted for factors including personal characteristics (e.g., age, physical illness, medication status) and different hormonal states across the prenatal periods.

Implications for eHealth and mHealth

Our findings suggest that the time-domain HRV parameters (e.g., rMSSD) can be a reliable, cost-effective, and easily used clinical indicator of emotional distress among pregnant women in the second trimester. In addition, the use of portable devices with a smartphone application (e.g., Elite HRV) for assessing ultra short-term (the 60 s) HRV parameters supports findings on the effectiveness of portable devices and smartphone applications for self-management during pregnancy to monitor women's mental health status. The Elite HRV application gives pregnant women and researchers tools that allow for the daily monitoring of HRV metrics on an individual level. The smartphone application (e.g., Elite HRV) is capable of collecting, analyzing, and exporting HRV data to the practitioners for further recording. This option would allow for the continuing biofeedback. Future research in the fields of eHealth and mHealth could explore whether HRV biofeedback, delivered via smartphone devices, can effectively reduce emotional distress levels in pregnant women. This non-invasive intervention would provide real-time information to women, allowing them to make subtle adjustments to reach the desired emotional state.

Conclusions

In summary, this study revealed that pregnant women's emotional distress was associated with lower levels of HRV time-domain parameters during their second pregnancy trimester. These findings support using HRV (especially referring to time-domain HRV parameters: rMSSD; SDNN; NN50) as a potential biomarker to predict pregnant women's emotional distress in the second trimester. In contrast, prenatal emotional distress showed no relationship to the HRV measurements in pregnant women during the first and third pregnancy trimesters. The fluctuation of physical and mental experiences during the first and third trimesters may confound the relationship between emotional distress and HRV.

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CRediT authorship contribution statement

Weiyi Xie: Writing – original draft. **Siu Man Ng:** Supervision, Conceptualization. **Clifton Robert Emery:** Writing – review & editing, Supervision. **Pingqiao Wang:** Project administration, Investigation, Formal analysis. **Hui Yun Li:** Writing – review & editing, Project administration, Investigation. **Amenda, M. WANG:** Writing – review & editing, Investigation, Formal analysis.

Declaration of Competing Interest

All authors have no known conflict of interest to disclose.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bionps.2024.100103.

References

Alam, T., Choudhary, A.K., Kumaran, S.D., 2018. Maternal heart rate variability during different trimesters of pregnancy. Natl. J. Physiol., Pharm. Pharmacol. 8 (11), 1475–1480. https://doi.org/10.5455/njppp.2018.8.0723327072018.

Alderdice, F., Lynn, F., 2011. Factor structure of the prenatal distress questionnaire. Midwifery *27* (4), 553–559. https://doi.org/10.1016/j.midw.2010.05.003.

Appelhans, B.M., Luecken, L.J., 2006. Heart rate variability as an index of regulated emotional responding. Rev. Gen. Psychol. *10* (3), 229–240. https://doi.org/10.1037/1089-2680.10.3.229.

Bennett, H.A., Einarson, A., Taddio, A., Koren, G., Einarson, T.R., 2004. Prevalence of depression during pregnancy: Systematic review. Obstet. Gynecol. *103* (4), 698–709. https://doi.org/10.1097/01.AOG.0000116689.75396.5f.

Bjelica, A., Cetkovic, N., Trninic-Pjevic, A., Mladenovic-Segedi, L., 2018. The phenomenon of pregnancy—A psychological view. Ginekol. Pol. *89* (2), 102–106. https://doi.org/10.5603/GP.a2018.0017.

Braeken, M.A.K.A., Jones, A., Otte, R.A., Widjaja, D., Van Huffel, S., Monsieur, G.J., Van den Bergh, B.R.H., 2015. Anxious women do not show the expected decrease in cardiovascular stress responsiveness as pregnancy advances. Biol. Psychol. *111*, 83–89. https://doi.org/10.1016/j.biopsycho.2015.08.007.

Brown, H., Krogh-Jespersen, S., Tandon, D., Graham, A., Mackiewicz Seghete, K., Wakschlag, L., 2021. Looking ahead: Pre-and perinatal interventions for maternal distress to prevent neurodevelopmental vulnerability. Prenat. Stress Child Dev. 595–622. https://doi.org/10.1007/978-3-030-60159-1_20.

Castaldo, R., Melillo, P., Bracale, U., Caserta, M., Triassi, M., Pecchia, L., 2015. Acute mental stress assessment via short term HRV analysis in healthy adults: A systematic review with meta-analysis. Biomed. Signal Process. Control *18*, 370–377. https://doi.org/10.1016/j.bspc.2015.02.012.

Caparros-Gonzalez, R.A., Romero-Gonzalez, B., Strivens-Vilchez, H., Gonzalez-Perez, R., Martinez-Augustin, O., Peralta-Ramirez, M.I., 2017. Hair cortisol levels, psychological stress and psychopathological symptoms as predictors of postpartum depression. PloS One *12* (8), e0182817. https://doi.org/10.1371/journal.pone.0182817.

Cattaneo, L.A., Franquillo, A.C., Grecucci, A., Beccia, L., Caretti, V., Dadomo, H., 2021. Is low heart rate variability associated with emotional dysregulation, psychopathological dimensions, and prefrontal dysfunctions? An integrative view. J. Pers. Med. *11* (9), 872. https://doi.org/10.3390/jpm11090872.

Challacombe, F.L., Pietikäinen, J.T., Kiviruusu, O., Saarenpää-Heikkilä, O., Paunio, T., Paavonen, E.J., 2023. Paternal perinatal stress is associated with children's emotional problems at 2 years. J. Child Psychol. Psychiatry 64 (2), 277–288. https://doi.org/10.1111/jcpp.13695.

Chan, K.P., 2015. Effects of perinatal meditation on pregnant Chinese women in Hong Kong: a randomized controlled trial. J. Nurs. Educ. Pract. *5* (1), 1–18. https://doi.org/10.5430/jnep.v5n1p1.

Chen, Y.S., Lu, W.A., Pagaduan, J.C., Kuo, C.D., 2020. A novel smartphone app for the measurement of ultra–short-term and short-term heart rate variability: validity and reliability study. JMIR mHealth uHealth *8* (7), e18761. https://doi.org/10.2196/18761.

Christian, L.M., 2012. Physiological reactivity to psychological stress in human pregnancy: Current knowledge and future directions. Prog. Neurobiol. *99* (2), 106–116. https://doi.org/10.1016/j.pneurobio.2012.07.003.

Dennis, C.L., Falah-Hassani, K., Shiri, R., 2017. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. Br. J. Psychiatry *210* (5), 315–323. https://doi.org/10.1192/bjp.bp.116.187179.

Dobbs, W.C., Fedewa, M.V., MacDonald, H.V., Holmes, C.J., Cicone, Z.S., Plews, D.J., Esco, M.R., 2019. The accuracy of acquiring heart rate variability from portable devices: a systematic review and meta-analysis. Sports Med. *49*, 417–435. https://doi.org/10.1007/s40279-019-01061-5.

Dostal, T., Plews, D.J., Hofmann, P., Laursen, P.B., Cipryan, L., 2019. Effects of a 12-week very-low carbohydrate high-fat diet on maximal aerobic capacity, high-intensity intermittent exercise, and cardiac autonomic regulation: non-randomized parallel-group study. Front. Physiol. *10*, 912. https://doi.org/10.3389/fphys.2019.00912.

Esco, M.R., Flatt, A.A., 2014. Ultra-short-term heart rate variability indexes at rest and post-exercise in athletes: evaluating the agreement with accepted recommendations. J. Sports Sci. Med. *13* (3), 535.

Faul, F., Erdfelder, E., Buchner, A., Lang, A.G., 2009. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. Behav. Res. Methods *41* (4), 1149–1160. https://doi.org/10.3758/BRM.41.4.1149.

Himariotis, A.T., Coffey, K.F., Noel, S.E., Cornell, D.J., 2022. Validity of a Smartphone Application in Calculating Measures of Heart Rate Variability. Sensors *22* (24), 9883. https://doi.org/10.3390/s22249883.

Hoogwegt, M.T., Pedersen, S.S., Theuns, D.A., Kupper, N., 2014. Relation between emotional distress and heart rate variability in patients with an implantable cardioverter-defibrillator. Psychophysiology *51* (2), 187–196. https://doi.org/10.1111/psyp.12158.

Ibrahim, S.M., Lobel, M., 2020. Conceptualization, measurement, and effects of pregnancy-specific stress: review of research using the original and revised Prenatal Distress Questionnaire. J. Behav. Med. *43* (1), 16–33. https://doi.org/10.1007/s10865-019-00068-7.

Jenkins, D.G., Quintana-Ascencio, P.F., 2020. A solution to minimum sample size for regressions. PloS One *15* (2), e0229345. https://doi.org/10.1371/journal.pone.0229345.

Guzik, P., Piekos, C., Pierog, O., Fenech, N., Krauze, T., Piskorski, J., Wykretowicz, A., 2018. Classic electrocardiogram-based and mobile technology derived approaches to heart rate variability are not equivalent. Int. J. Cardiol. *258*, 154–156. https://doi.org/10.1016/j.ijcard.2018.01.056.

Kim, H.-G., Cheon, E.-J., Bai, D.-S., Lee, Y.H., Koo, B.-H., 2018. Stress and heart rate variability: A meta-analysis and review of the literature. Psychiatry Investig. *15* (3), 235–245. https://doi.org/10.30773/pi.2017.08.17.

Kimmel, M.C., Fransson, E., Cunningham, J.L., Brann, E., Grewen, K., Boschiero, D., Chrousos, G.P., Meltzer-Brody, S., Skalkidou, A., 2021. Heart rate variability in late pregnancy: Exploration of distinctive patterns in relation to maternal mental health. Transl. Psychiatry *11* (1), 286. https://doi.org/10.1038/s41398-021-01401-y.

Kuo, C.D., Chen, G.Y., Yang, M., Lo, H., Tsai, Y., 2000. Biphasic changes in autonomic nervous activity during pregnancy. Br. J. Anaesth. *84* (3), 323–329. https://doi.org/10.1093/oxfordjournals.bja.a013433.

Malik, M., 1996. Heart Rate Variability. Ann. Noninvasive Electrocardiol. *1* (2), 151–181. https://doi.org/10.1111/j.1542-474X.1996.tb00275.x.

Manzari, N., Matvienko-Sikar, K., Baldoni, F., O'Keeffe, G.W., Khashan, A.S., 2019. Prenatal maternal stress and risk of neurodevelopmental disorders in the offspring: A systematic review and meta-analysis. Soc. Psychiatry Psychiatr. Epidemiol. *54* (11), 1299–1309. https://doi.org/10.1007/s00127-019-01745-3.

McDonald, S.W., Lyon, A.W., Benzies, K.M., McNeil, D.A., Lye, S.J., Dolan, S.M., Pennell, C.E., Bocking, A.D., Tough, S.C., 2013. The All Our Babies pregnancy cohort: Design, methods, and participant characteristics. BMC Pregnancy Childbirth *13* (1), S2. https://doi.org/10.1186/1471-2393-13-S1-S2.

Mizuno, T., Tamakoshi, K., Tanabe, K., 2017. Anxiety during pregnancy and autonomic nervous system activity: A longitudinal observational and cross-sectional study. J. Psychosom. Res. *99*, 105–111. https://doi.org/10.1016/j.jpsychores.2017.06.006.

Moya-Ramon, M., Mateo-March, M., Peña-González, I., Zabala, M., Javaloyes, A., 2022. Validity and reliability of different smartphones applications to measure HRV during short and ultra-short measurements in elite athletes. Comput. Methods Prog. Biomed. *217*, 106696 https://doi.org/10.1186/s12911-019-0742-y.

Ng, S., Leng, L.L., Chan, K.P., Lo, H.H., Yeung, A., Lu, S., Wang, A., Li, H.Y., 2022. Study protocol of guided mobile-based perinatal mindfulness intervention (GMBPMI)—A randomized controlled trial. PLOS ONE *17* (7), e0270683. https://doi.org/10.1371/journal.pone.0270683.

Okagbue, H.I., Adamu, P.I., Bishop, S.A., Oguntunde, P.E., Opanuga, A.A., Akhmetshin, E.M., 2019. Systematic Review of Prevalence of Antepartum Depression during the Trimesters of Pregnancy. Open Access Maced. J. Med. Sci. *7* (9), 1555–1560. https://doi.org/10.3889/oamjms.2019.270.

Perrotta, A.S., Jeklin, A.T., Hives, B.A., Meanwell, L.E., Warburton, D.E., 2017. Validity of the elite HRV smartphone application for examining heart rate variability in a field-based setting. J. Strength Cond. Res. *31* (8), 2296–2302. https://doi.org/10.1519/JSC.0000000000001841.

Riddle, J.N., Jager, L., Sherer, M.L., Pangtey, M., Osborne, L.M., 2023. Anxiety in pregnancy and stress responsiveness: An exploratory study of heart rate variability, cortisol, and alpha-amylase in the third trimester. J. Neuroendocrinol. *35* (7) https://doi.org/10.1111/jne.13238.

Romero-Gonzalez, B., Caparros-Gonzalez, R.A., Gonzalez-Perez, R., Delgado-Puertas, P., Peralta-Ramirez, M.I., 2018. Newborn infants' hair cortisol levels reflect chronic maternal stress during pregnancy. PLoS One *13* (7), e0200279. https://doi.org/10.1371/journal.pone.0200279.

Rouleau, C.R., Tomfohr-Madsen, L.M., Campbell, T.S., Letourneau, N., O'Beirne, M., Giesbrecht, G.F., 2016. The role of maternal cardiac vagal control in the association between depressive symptoms and gestational hypertension. Biol. Psychol. *117*, 32–42. https://doi.org/10.1016/j.biopsycho.2016.02.002.

Sarhaddi, F., Azimi, I., Axelin, A., Niela-Vilén, H., Liljeberg, P., Rahmani, A.M., 2022. Trends in heart rate and heart rate variability during pregnancy and the 3-Month Postpartum Period: Continuous monitoring in a free-living context. Jmir Mhealth Uhealth *10* (6), e33458. https://doi.org/10.2196/33458.

Schlicht, E., Caruso, R., Denby, K., Matias, A., Dudar, M., Ives, S.J., 2018. Effects of wrist cooling on recovery from exercise-induced heat stress with Firefighting personal protective equipment. J. Occup. Environ. Med. *60* (11), 1049. https://doi.org/10.1097/JOM.0000000000001436.

Schumann, A., de la Cruz, F., Köhler, S., Brotte, L., Bär, K.J., 2021. The influence of heart rate variability biofeedback on cardiac regulation and functional brain connectivity. Front. Neurosci. *15*, 691988 https://doi.org/10.3389/fnins.2021.691988.

Seltzer, H., Pellman, M., Warchock, R., Billian, J., Baker, R., 2021. Mobile evaluation of heart rate variability using the diver's reflex. NeuroRegulation *8* (2), 96–103. https://doi.org/10.15540/nr.8.2.96.

Setse, R., Grogan, R., Pham, L., Cooper, L.A., Strobino, D., Powe, N.R., Nicholson, W., 2009. Longitudinal study of depressive symptoms and health-related quality of life during pregnancy and after delivery: the Health Status in Pregnancy (HIP) study. Matern. Child Health J. *13*, 577–587. https://doi.org/10.1007/s10995-008-0392-7.

Shaffer, F., Ginsberg, J.P., 2017. An overview of heart rate variability metrics and norms. Front. Public Health *5*, 258. https://doi.org/10.3389/fpubh.2017.00258.

Shaffer, F., Shearman, S., Meehan, Z.M., 2016. The promise of ultra-short-term (UST) heart rate variability measurements. Biofeedback *44* (4), 229–233. https://doi.org/10.5298/1081-5937-44.3.09.

Shea, A.K., Kamath, M.V., Fleming, A.S., Streiner, D.L., Redmond, K., Steiner, M., 2008. The effect of depression on heart rate variability during pregnancy. Clin. Auton. Res. *18* (4), 203–212. https://doi.org/10.1007/s10286-008-0480-1.

Solanki, J.D., Desai, F.H., Desai, K.H., 2020. Heart rate variability is reduced in normal pregnancy irrespective of trimester: A cross-sectional study from Gujarat, India. J. Fam. Med. Prim. Care *9* (2), 626. https://doi.org/10.4103/jfmpc.jfmpc_1123_19.

Solorzano, C.S., Violani, C., Grano, C., 2022. Pre-partum HRV as a predictor of postpartum depression: The potential use of a smartphone application for physiological recordings. J. Affect. Disord. *319*, 172–180. https://doi.org/10.1016/j.jad.2022.09.056.

Tang, X., Lu, Z., Hu, D., Zhong, X., 2019. Influencing factors for prenatal stress, anxiety and depression in early pregnancy among women in Chongqing, China. J. Affect. Disord. *253*, 292–302. https://doi.org/10.1016/j.jad.2019.05.003.

Türk, R., Sakar, T., Erkaya, R., 2017. The effect of pregnancy on happiness. Procedia-Soc. Behav. Sci. *237*, 1247–1253. https://doi.org/10.1016/j.sbspro.2017.02.198.

Vondrasek, J.D., Riemann, B.L., Grosicki, G.J., Flatt, A.A., 2023. Validity and Efficacy of the Elite HRV Smartphone Application during Slow-Paced Breathing. Sensors *23* (23), 9496. https://doi.org/10.3390/s23239496.

World Health Organization (WHO). (2019). Mental health: maternal mental health. Available from: ⟨https://www.who.int/teams/mental-health-and-substance-use/promotion-prevention/maternal-mental-health⟩.

Wu, S., Zhang, K., Parks-Stamm, E.J., Hu, Z., Ji, Y., Cui, X., 2021. Increases in anxiety and depression during COVID-19: a large longitudinal study from China. Front. Psychol. *12* https://doi.org/10.3389/fpsyg.2021.706601.

Yali, A.M., Lobel, M., 1999. Coping and distress in pregnancy: An investigation of medically high risk women. J. Psychosom. Obstet. Gynecol. *20* (1), 39–52. https://doi.org/10.3109/01674829909075575.

Yuksel, F., Akin, S., Durna, Z., 2013. Prenatal distress in T urkish pregnant women and factors associated with maternal prenatal distress. J. Clin. Nurs. *23* (1-2), 54–64. https://doi.org/10.1111/j.1365-2702.2012.04283.x.