

# Sympathovagal Imbalance, Cardiometabolic Risks and Hypertension Status are Linked to Depression in Women Having Risk Factors for Pregnancy-induced Hypertension

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## ABSTRACT

**Background and Aim:** Pregnancy is a physiological state in which there are cardiovascular, autonomic, hemodynamic and psychological changes. Increase in incidence of stress and depression in antenatal period has been reported. Autonomic changes in pregnancy-induced hypertension (PIH) and its dysfunction in depression are well documented. However, there is no report of contribution of sympathovagal imbalance (SVI) and cardiometabolic alterations to stress and depression in PIH. **Methods:** In this case-control study, we assessed and analyzed cardiovascular autonomic functions including heart rate variability (HRV) and cardiometabolic risks (CMR) between pregnant women having risks of PIH ( $n=62$ ) and normal healthy pregnant women ( $n=68$ ). The perceived stress scale (PSS-10) and Quality of Life (QoL) were used to evaluate depressive symptoms and perceived stress. The HRV and CMR parameters were correlated with PSS. Multiple regression analysis was performed individually to study their association with PSS. Logistic regression was done to determine the prediction of hypertension/prehypertension status by PSS. **Results:** There was increase in heart rate and blood pressure, decreased HRV and increased markers of insulin resistance, atherogenic lipid profile, markers of inflammation, oxidative stress and vascular endothelial dysfunction in PIH risk subjects compared to control subjects. Parameters of SVI and decreased cardiovagal modulation and CMR were significantly correlated and associated with PSS. PSS had independent prediction of prehypertension/hypertension status in the study group. **Conclusion:** Findings of the present study indicate that there is considerable SVI and CMR in PIH. It appears that depression is the major cause of SVI and decreased cardiovagal modulation in PIH, and retrograde inflammation and vascular endothelial dysfunction could be the potential mechanisms of depression mediated SVI in PIH.

**Key words:** Pregnancy-induced hypertension, Sympathovagal imbalance, Cardiovagal inhibition, Depression, Perceived stress scale, Cardiometabolic risks.

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## INTRODUCTION

Pregnancy is associated with multiple physiological and behavioral changes that predispose pregnant women to many health conditions detrimental to maternal and child well-being.<sup>[1]</sup> Diagnostic and statistical manual of mental disorders 5 (DSM 5) recognise peripartum depression as a major depressive episode (MDD) occurring during or after pregnancy.<sup>[2]</sup> Antenatal depression in coastal South has been reported to be 16.3%,<sup>[3]</sup> and similar results were obtained by Rahman A *et al.*, who found prevalence of perinatal mental disorders to be 15.6% in low and middle income countries in a meta-analysis study.<sup>[4]</sup> As demonstrated in various studies, perinatal depression is associated with poor maternal and foetal outcomes.<sup>[3,5]</sup> In these studies, Perceived Stress Scale (PSS),<sup>[6]</sup> was used for assessing stress of pregnant women.<sup>[3-5]</sup> Recently we have reported association of sympathovagal imbalance (SVI), decreased baroreflex sensitivity (BRS) and

increased cardiovascular (CV) risks with depression in pregnant women assessed by PSS.<sup>[7]</sup> It has been reported that depression is more in women having hypertension during pregnancy.<sup>[8,9]</sup>

Pregnancy-induced hypertension (PIH) is one of the most common causes of maternal morbidity and mortality.<sup>[10]</sup> It has been estimated that around 5-10 % of women develop hypertension during pregnancy.<sup>[11]</sup> PIH is categorized as chronic hypertension, preeclampsia, eclampsia, preeclampsia superimposed on chronic hypertension and gestational hypertension without proteinuria.<sup>[10]</sup> Depression during pregnancy is so great that World Health Organization (WHO) recognizes depression as one of the major causes of morbidity and disability among young female adults.<sup>[12]</sup> Both hypertension and depression place women in greater need of care, since these conditions can lead to important dysfunctions in the body. Furthermore, the

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association between depression and hypertension is an important factor that should be evaluated early and treated effectively during pregnancy. Reports indicate that psychological factors such as depression and/or depressive symptoms associated with gestational hypertension have increased greatly in recent years.<sup>[13,14]</sup> However, till date mechanisms that aggravate depression in PIH and the factors that precipitate depressive symptoms in pregnancy have not been systematically elucidated.

We have reported sympathovagal imbalance (SVI), decreased baroreflex sensitivity (BRS) and increased cardiovascular (CV) risks in pregnancy-induced hypertension (PIH).<sup>[15-18]</sup> Autonomic imbalance has been reported to be associated with depression.<sup>[19,20]</sup> However, till date the link of PSS to sympathovagal imbalance in pregnancy and PIH has not been assessed. Therefore, this study was conducted to evaluate if there any association between depression and hypertensive disorders status, and if SVI contributes to depression in PIH.

## MATERIALS AND METHODS

The present case-control study was conducted in the Department of Physiology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India. After obtaining approval of the project plan from research and ethics committees of JIPMER, 140 subjects (68 in control group, 72 in study group) were recruited from the Outpatient Department (OPD) of the Obstetrics and Gynecology department of JIPMER during the period of January, 2010 to December, 2012. Written informed consent was obtained from all the participants prior to initiation of the study.

### Inclusion and Exclusion Criteria

Subjects of study group included pregnant women who had risk factors for PIH. The subjects of control group included normal pregnant women without having risk factors for PIH. Inclusion criteria of risk factors for PIH were kept same as reported earlier,<sup>[15]</sup> such as family history of preeclampsia, preeclampsia in previous pregnancy, extremes of reproductive age, body mass index (BMI) > 35, diastolic blood pressure (DBP) > 80 mm Hg at the first visit, first pregnancy, multiple pregnancy, underlying medical conditions (diabetes mellitus, renal disease pre-existing hypertension) etc. Pregnant women having any other medical illness or receiving medications for other problems were excluded from the study.

### Patient Recruitment and Baseline Measurements

The subjects attending obstetrics OPD for their regular check-ups in the third trimester of gestation were recruited for the study. They were reported to polygraph laboratory of physiology department for recording of various parameters at 36 to 38 weeks of pregnancy, about two hours after a light breakfast devoid of coffee or tea. Height and weight were measured to calculate body mass index (BMI). Blood pressure (BP) was recorded using the automatic non-invasive BP monitor, Omron, HEM 7203 model (Omron Healthcare Co., Kyoto, Japan). Heart rate, systolic BP and diastolic BP were noted from the display screen of BP monitor, and mean arterial pressure (MAP) was calculated. Rate pressure product (RPP) was calculated using the formula,  $RPP = \text{systolic pressure} \times \text{heart rate} \times 10^{-2}$ .<sup>[21]</sup>

### Estimation of Biochemical Parameters

Five ml of venous blood was collected from all the subjects of both the groups in all the three trimesters for estimation of fasting blood glucose (FBG), serum insulin, lipid profile (TC: Total serum cholesterol; TG: Triglyceride; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein), malonaldehyde (MDA), by using biochemistry autoanalyzer. HOMA-IR and atherogenic index (AI) were calculated. Inflammatory

markers such as high-sensitive C-reactive protein (hsCRP) (Calbiotech, USA), tumour necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6) (Diaclone, France), were measured using ELISA kit according to manufacturer instructions. Nitric oxide derivatives (nitrate and nitrite) and endothelin 1 (ET-1) were estimated using chemical method (Elabscience, USA).

### HRV Recording

Following 10 min of supine rest in polygraph laboratory (room temperature maintained at 25°C), basal heart rate (BHR) and blood pressures (diastolic and systolic) were recorded. For recording of short-term HRV, recommendation of the Task Force on HRV and our previous methodology of HRV recording were followed.<sup>[15,22]</sup> For the purpose, ECG electrodes were connected and Lead II ECG was acquired at a rate of 1000 samples/second during supine rest using BIOPAC MP 100 data acquisition system (BIOPAC Inc., USA). The data was transferred from BIOPAC to a windows-based PC with Acqknowledge software version 3.8.2. Ectopics and artifacts were removed from the recorded ECG. RR tachogram was extracted from the edited 256 sec ECG using the R wave detector in the Acqknowledge software and saved in ASC-II format which was later used offline for short term HRV analysis. HRV analysis was done using the HRV analysis software version 1.1 (Bio-signal Analysis group, Finland). Variance, defined as power in a portion of the total spectrum of frequencies was measured in milliseconds squared ( $\text{ms}^2$ ). Frequency-domain indices of HRV such as total power (TP), normalized low-frequency power (LFnu), normalized high-frequency power (HFnu), ratio of low-frequency to high-frequency power (LF-HF ratio), and time-domain indices such as square root of the mean of the sum of the squares of the differences between adjacent NN intervals (RMSSD), standard deviation of normal to normal interval (SDNN), number of interval differences of successive NN intervals greater than 50 ms (NN50) and the proportion derived by dividing NN50 by the total number of NN intervals (pNN50) were recorded.

### Assessment of Depression by PSS-10 and Quality of Life Scale

The level of depression was assessed using Perceived Stress Scale (PSS-10),<sup>[23]</sup> and Quality of Life scale (QoL).<sup>[24]</sup> The PSS-10 is a 10 items self-reporting questionnaire with each response scored from 0 to 4 points and total scores ranged from 0 to 40 points. PSS-10 scores are classified from 0 to 13 (low), 14–26 (moderate), and 27–40 (severe perceived stress). For QoL scale, subjects are asked to indicate on a 4-point scale how often in the past week they have felt in accordance with 11 different statements. Responses are summed for a total score, higher scores indicating more depressive symptomology. In the present study, Flanagan Quality of Life (QoL) scale was used to assess the quality of life of the participants. It is composed of 16 items which covers 5 domains. The domains include physical and material well-being; relations with other people; social, community and civic activities; personal development and fulfilment; and recreation. This questionnaire is a 7-point scale ranging from delighted to terrible. The total score ranges from 16-112. The average total score for healthy population is about 90.

### Statistical Analysis of Data

SPSS version 13 (SPSS Software Inc., Chicago, IL, USA) was used for statistical analysis. All the data were expressed as mean $\pm$ SD. Normality of data was tested by Kolmogorov Smirnov test. For parametric data, the level of significance between the groups was tested by Student's unpaired *t* test and for nonparametric data Welch's corrected *t* test was used. The independent contribution of various parameters of cardiometabolic risks to PSS-10 was assessed by multiple regression analysis. Independent prediction of PSS-10 to hypertension status in third trimester was

assessed by multivariate logistic regression. The p value less than 0.05 was considered statistically significant.

## RESULTS

There was no significant difference in age of subjects of both the groups. BMI, BHR, BP and RPP in the study group were significantly more ( $P < 0.0001$ ) at 36<sup>th</sup> week compared to the control group (Table 1). Among the HRV indices, the TP, HFnu and time-domain indices (RMSSD, SDNN, NN50, pNN50) were significantly reduced ( $P < 0.0001$ ) and LFnu and LF-HF ratio were significantly increased ( $P < 0.0001$ ) in study group compared to control group (Table 1). All blood glucose-related parameters including HOMA-IR, lipid profile (except HDL) and lipid risk factors, inflammatory and oxidative stress markers were significantly high in study group compared to control group (Table 2). Endothelin-1 was significantly increased and NO was significantly decreased in study group compared to control group (Table 2). The PSS score significantly increased and QoL was significantly decreased in study group compared to control group (Table 2).

There was no significant correlation of any of the parameter with PSS in control group (Table 3). In study group, except BMI, hsCRP and

MDA, all parameters were significantly correlated with PSS. On multiple regression analysis demonstrated independent contribution of RPP, TP, LF-HR ratio, IL-6, TNF- $\alpha$ , endothelin-1, and NO to PSS (Table 4). However, there was no significant contribution of HOMA-IR, AI and MDA to PSS.

On multivariate logistic regression analysis to determine the predictive power of PSS in the development of hypertension or prehypertension status, it was found the significance of prediction was more in control group ( $P = 0.003$ ) compared to study group ( $P = 0.006$ ) (Table 5).

## DISCUSSION

In the present study, PSS significantly predicted the prehypertension and hypertension status in study group subjects (Table 5), which indicates that the level of depression is directly linked to the rise in BP in pregnant

**Table 1: Age, BMI and cardiovascular parameters including HRV in control group (normal pregnant women without having risk factors of pregnancy-induced hypertension) and study group (pregnant women having risk factors for pregnancy-induced hypertension), at 36<sup>th</sup> week of pregnancy.**

	Control group (n=68)	Study group (n=72)	P value
Age (Yrs)	27.58±3.52	26.85±4.10	3.5680
Weight (Kg)	65.50±5.24	71.86±5.74	0.0002
BMI (Kg/m <sup>2</sup> )	25.72±3.10	28.92±4.75	<0.0001
BHR (per min)	82.86±8.50	95.25±9.50	<0.0001
SBP (mmHg)	110.56±10.42	131.98±12.36	<0.0001
DBP (mmHg)	71.08±6.25	86.42±8.70	<0.0001
RPP (mmHg/min)	91.60±9.40	125.70±13.15	<0.0001
<b>HRV Parameters</b>			
TP (ms <sup>2</sup> )	772.20±267.45	438.25±120.20	<0.0001
LFnu	45.80±17.22	62.25±20.32	<0.0001
HFnu	54.20±18.24	37.75±12.50	<0.0001
LF-HF ratio	0.84±0.28	1.64±0.49	<0.0001
RMSSD	44.53±18.70	25.37±7.42	<0.0001
SDNN	40.40±15.45	20.22±6.86	<0.0001
NN50	44.40±17.35	21.50±7.68	<0.0001
pNN50	22.13±9.40	10.21±3.53	<0.0001

The data presented are mean±SD. Comparison was done using Student's unpaired *t* test. *P* value <0.05 was considered statistically significant. BMI: Body mass index; BHR: Basal heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RPP: Rate-pressure product; TP: Total power of HRV; LFnu: Normalized low-frequency (LF) power; HFnu: Normalized high-frequency (HF) power; RMSSD: The square root of the mean of the sum of the squares of the differences between adjacent NN intervals; SDNN: Standard deviation of normal to normal interval; NN50: The number of interval differences of successive NN intervals greater than 50; pNN50: The proportion derived by dividing NN50 by the total number of NN intervals.

**Table 2: Biochemical parameters, PSS and QoL scores in control and study groups in third trimester of gestation.**

	Control group (n=68)	Study group (n=72)	P value
<b>Glucose related parameters</b>			
FBG (mg/dL)	81.20±10.56	110.70±10.30	<0.0001
Insulin ( $\mu$ U/mL)	5.30±1.68	19.30±3.85	<0.0001
HOMA-IR	1.25±0.31	5.30±1.12	<0.0001
<b>Lipid related parameters</b>			
TC (mg/dL)	148.80±25.20	170.80±27.20	<0.0001
TG (mg/dL)	81.70±17.40	120.76±22.30	<0.0001
LDL (mg/dL)	87.50±19.10	125.30±24.50	<0.0001
VLDL (mg/dL)	16.21±3.45	25.08±5.06	<0.0001
HDL (mg/dL)	48.17±5.35	34.42±4.58	<0.0001
TC/HDL	3.07±0.42	4.97±0.68	<0.0001
TG/HDL	1.70±0.25	3.50±0.52	<0.0001
Atherogenic index	0.23±0.08	0.57±0.11	<0.0001
<b>Inflammatory and OS parameters</b>			
hsCRP (ng/dL)	396.40±65.20	948.30±178.20	<0.0001
IL-6 (pg/ml)	72.25±8.68	135.60±12.30	<0.0001
TNF- $\alpha$ (pg/ml)	152.80±13.32	284.55±18.35	<0.0001
MDA ( $\mu$ M/L)	1.86±0.45	5.47±0.98	<0.0001
<b>Endothelial dysfunction parameters</b>			
Endothelin-1 ( $\mu$ g/L)	6.86±0.85	10.22±0.1.07	<0.0001
NO ( $\mu$ mol/L)	32.15±3.46	21.05±2.85	<0.0001
<b>Depression parameters</b>			
PSS	15.10±3.60	21.83±5.52	0.0001
QoL	102.56±9.20	86.21±7.90	0.0001

The data presented are mean±SD. Comparison was done using Student's unpaired *t* test. *P* value <0.05 was considered statistically significant. FBG: Fasting blood glucose; HOMA-IR: homeostatic model assessment of insulin resistance; TC: Total serum cholesterol; TG: Triglyceride; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein; OS: Oxidative stress; hsCRP: high-sensitive C reactive protein; IL-6: Interleukin 6; TNF- $\alpha$ : Tumour necrosis factor  $\alpha$ ; MDA: Malondialdehyde; NO: Nitric oxide; PSS: Perceived stress scale; QoL: Quality of life.

**Table 3: Correlation of PSS with various cardiometabolic parameters in both control and study group in 3<sup>rd</sup> trimester of pregnancy.**

	Control group		Study group	
	r	P	r	P
BMI	- 0.082	0.391	0.105	0.341
BHR	- 0.180	0.091	0.268	0.040
SBP	- 0.179	0.092	0.305	0.012
RPP	- 0.195	0.072	0.327	0.009
TP	0.210	0.077	- 0.386	0.005
LH-HF ratio	- 0.205	0.080	0.260	0.043
HOMA-IR	- 0.236	0.058	0.437	0.001
Atherogenic index	- 0.240	0.057	0.430	0.001
hs-CRP	- 0.182	0.091	0.240	0.056
IL-6	- 0.180	0.092	0.305	0.012
TNF-α	- 0.196	0.072	0.327	0.009
MDA	- 0.095	0.294	0.196	0.091
Endothelin-1	- 0.203	0.081	0.350	0.007
NO	0.246	0.055	- 0.480	0.000

The p values less than 0.05 was considered significant. PSS: Perceived stress scale; BMI: Body mass index; WHR: Waist-hip ratio; BHR: Basal heart rate; SBP: Systolic blood pressure; RPP: Rate-pressure product; TP: Total power of HRV; LF-HF ratio: Ratio of normalized low-frequency (LF) power normalized high-frequency (HF) power; HOMA-IR: homeostatic model assessment of insulin resistance; hsCRP: high-sensitive C reactive protein; IL-6: Interleukin 6; TNF-α: Tumour necrosis factor α; MDA: Malondialdehyde; NO: nitric oxide.

**Table 4: Multiple regression analysis to assess independent contribution of various important cardiometabolic parameters to PSS (as dependent variable) in third trimester in the study group.**

Independent variables	Standardized regression coefficient	Confidence interval		P value
		Lower limit	Upper limit	
RPP	0.327	0.021	0.108	0.011
TP	-0.416	0.002	0.185	0.007
LF-HF ratio	0.308	- 0.032	0.156	0.025
HOMA-IR	0.122	0.015	0.005	0.104
AI	0.157	0.005	0.088	0.092
IL-6	0.292	- 0.003	0.145	0.031
TNF-α	0.308	0.032	0.206	0.025
MDA	0.244	0.001	0.072	0.062
Endothelin-1	0.315	0.033	0.134	0.018
NO	-0.300	- 0.002	0.135	0.027

P values < 0.05 were considered significant. RPP: Rate-pressure product; TP: Total power of HRV; LF-HF ratio: Ratio of normalized low-frequency (LF) power normalized high-frequency (HF) power; HOMA-IR: homeostatic model assessment of insulin resistance; AI: Atherogenic index; IL-6: Interleukin 6; TNF-α: Tumour necrosis factor α; MDA: Malondialdehyde; NO: nitric oxide.

**Table 5: Univariate logistic regression analysis of PSS (as dependent variable) with prehypertension / hypertension status (as independent variables) in study group population at 36<sup>th</sup> week of gestation, adjusted for age, gender and BMI.**

	OR (95% C.I.)	P value
Study Group	3.86 (1.45 to 10.582)	0.004

P < 0.05 considered significant; PSS: Perceived stress score; BMI: Body mass index; OR: Odds ratio.

women having risk of developing PIH at 36<sup>th</sup> week of gestation. As such PSS was significantly high and QOL was significantly low in the study group, indicating that the high-risk pregnant women had higher degrees of depression compared to the normal pregnant women. There are reports of association between depression and the higher risk of gestational hypertension. In general, women with depressive symptoms were more likely to develop hypertensive disorders of pregnancy. Reports have revealed the association between depressions with a moderately increased risk of preeclampsia.<sup>[25]</sup>

The BHR was significantly high in study group compared to control group (Table 1). Heart rate at rest is the function of vagal tone and increase in HR (resting tachycardia) represents decreased vagal activity.<sup>[26]</sup> Recently it has been reported that increase in resting heart rate is a cardiometabolic risk and risk factor for all-cause mortality.<sup>[27]</sup> Thus, significantly increase in BHR in study group at 36<sup>th</sup> week of pregnancy compared to control group indicates increased CV risks in these subjects in later part of pregnancy. The level of blood pressure is the function of vascular resistance that reflects the sympathetic tone.<sup>[28]</sup> Thus increase in SBP and DBP in study group subjects compared to control group subjects indicates the increase sympathetic tone in pregnant women with risk factors for PIH. RPP is a measure of myocardial work load and oxygen utilization.<sup>[21]</sup> Increased RPP, especially in individuals with high blood pressure has been reported as a potential CV risk.<sup>[29]</sup> Thus, increased BP, resting tachycardia and increased RPP in study group subjects compared to control group subjects could predispose women with risk of PIH to CV risk in their peripartum period. RPP had independent contribution to PSS, indicating that myocardial work stress could be linked to the level of depression in these high-risk women.

LF-HF ratio is the index of SVI and increase in this ratio reflects increased sympathetic activity.<sup>[22]</sup> LF-HF ratio was significantly high in study group in comparison to control group, which confirms the presence of sympathetic overactivity in subjects with risks for PIH. There was decrease in time domain indices (RMSSD, SDNN, NN50 and pNN50) in study group subjects indicating decreased vagal drive in pregnant women having risk of PIH. TP in general represents the magnitude of heart rate variability and the vagal potency of cardiac drive.<sup>[22]</sup> Decrease in HRV (decreased TP) has recently been reported to be associated with cardiac morbidity and sudden cardiac death.<sup>[30]</sup> In the present study, TP was significantly less in study group subjects in 3<sup>rd</sup> trimesters of pregnancy. Thus, pregnant women with risk for PIH are at greater risk of cardiac morbidities and mortalities. TP and LF-HF ratio were significantly correlated and associated with PSS. These findings indicate that SVI and decreased HRV are linked the level of depression in PIH.

Though the exact cause of decreased SVI in study group can be ascertained from the present study, one may propose that body weight and BMI in these subjects could be the mechanism for it, as increased adiposity has been reported to increase sympathetic and decrease vagal activity.<sup>[31,32]</sup> Another important risk factor for gestational hypertension cited in some of studies is the association not only with depression,

but also with high BMI. Obesity and depression have been cited as the most prevalent comorbidities of gestation.<sup>[33]</sup> However, the correlation between higher BMI associated to depression and the development of gestational hypertension has not been fully established yet. Moreover, in the present study, there was no correlation of BMI with PSS in the study group.

However, the increased sympathovagal imbalance (increased LF-HF ratio) and decreased cardiovagal modulation (decreased TP) at 3<sup>rd</sup> trimester in study group could be due to insulin resistance, atherogenic lipid profile, retrograde inflammation and oxidative stress, as HOMA-IR, AI, hsCRP, IL-6, TNF- $\alpha$  and MDA were significantly high in study group subjects compared to control subjects (Table 2). Further, these parameters except hsCRP were significantly correlated with PSS (Table 3). However, only IL-6 and TNF- $\alpha$  had independent contribution to PSS (Table 4). Thus, it appears that inflammation is a major contributor to depression in PIH. As such, inflammation has been reported to be involved in the pathophysiology of depression.<sup>[34]</sup>

Increased endothelin-1 and decreased NO are the markers of vascular endothelial dysfunction and vascular inflammation.<sup>[35]</sup> In the present study, endothelin-1 was significantly increased and NO was significantly decreased in study group (Table 1), and both of them were significantly correlated with PSS (Table 3) and had independent association with PSS (Table 4). Recently, biomarkers of vascular inflammation have been implicated in the causation of depression.<sup>[36]</sup> Recently we have also reported the role of decreased NO in the development of CV risks in gestational hypertension.<sup>[37]</sup> Further, decreased brain NO synthase expression has been reported in depression.<sup>[38]</sup> Therefore, decreased NO production might possibly be among the mechanisms of depression in PIH. Thus, from findings of the present study it appears that depression is the major cause of SVI and decreased cardiovagal modulation in PIH and retrograde inflammation and vascular endothelial dysfunction could be the potential mechanisms of depression-mediated SVI in PIH.

## CONCLUSION

Findings of the present study indicate that there is considerable sympathovagal imbalance and increased cardiometabolic risks in PIH. It is likely that the depression is the major cause of SVI and decreased cardiovagal modulation in PIH, and retrograde inflammation and vascular endothelial dysfunction could be the potential mechanisms of depression mediated SVI in PIH.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**PIH:** Pregnancy-induced Hypertension; **SVI:** Sympathovagal Imbalance; **HRV:** Heart Rate Variability; **CMR:** Cardiometabolic Risks; **PSS:** Perceived Stress Scale; **QoL:** Quality of Life; **BRS:** Baroreflex Sensitivity; **TC:** Total Cholesterol; **TG:** Triglyceride; **LDL:** Low-density Lipoprotein; **VLDL:** Very Low-density Lipoprotein; **MDA:** Malondialdehyde; **AI:** Atherogenic Index; **hsCRP:** High-Sensitive C-Reactive Protein; **TNF- $\alpha$ :** Tumour Necrosis Factor  $\alpha$ ; **IL-6:** Interleukin-6; **RPP:** Rate-pressure product; **TP:** Total Power; **LFnu:** Normalized Low Frequency Power; **HFnu:** Normalized High Frequency Power; **RMSSD:** The Square Root of the Mean of the Sum of the Squares of the Differences Between Adjacent NN Intervals; **SDNN:** Standard Deviation of Normal to Normal Interval;

**NN50:** The Number of Interval Differences of Successive NN Intervals Greater than 50; **pNN50:** The Proportion Derived by Dividing NN50 by the Total Number of NN Intervals.

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