

Original Research Article

Magnitude of sympathovagal imbalance and its correlation with inflammatory response and oxidative stress in pregnant women at risk of pregnancy induced hypertension: a cross-sectional study

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ABSTRACT

Background: Pregnancy-induced hypertension (PIH) is a common complication of pregnancy but its genesis isn't known. It is proposed to be due to an excessive inflammatory response in the mother secondary to placental or maternal factors. The study aimed to measure the magnitude of sympathovagal imbalance (SVI) and to evaluate the role that oxidative stress and the inflammatory response play in the development of sympathovagal imbalance in pregnant mothers with risk factors of pregnancy-induced hypertension.

Methods: A cross-sectional study was carried out among pregnant women with at least one risk factor for PIH and age-matched pregnant women without risk factors for PIH as controls from March 2023 to February 2024 in a tertiary care hospital in Pondicherry. The intergroup differences in the mean between the two groups were compared using the Mann Whitney test and the Student's T-test.

Results: Short-term heart rate variability was significantly higher among cases while time domain analysis didn't show significance. Total Cholesterol (TC), Triglycerides (TG), Very Low-Density Lipoprotein (VLDL) and Low-Density Lipoprotein (LDL) were significantly higher among the cases and High-Density Lipoprotein (HDL) was low in cases compared to controls. There is a strong correlation of Low Frequency to High Frequency (LF-HF) ratio with Tumor Necrosis Factor-alpha (TNF- α) and high sensitivity (hs-CRP) in patients with risk factors of PIH.

Conclusions: Pregnant women at risk of pregnancy-induced hypertension showed increased inflammatory response, oxidative stress and dyslipidaemia. Hence, conducting sessions for stress management not only during pregnancy but also in the pre-pregnancy period can alleviate sympathetic dysfunction.

Keywords: Gestational hypertension, High-risk pregnancy, Pregnancy-induced hypertension

INTRODUCTION

Hypertensive disorders are diagnosed in 5 to 10% of all pregnancies. Pregnancy induced hypertension (PIH) occupy 47.4% of these complications.¹ It is defined as "Hypertension that occurs after 20 weeks of gestation in

women with previously normal blood pressure".² It contributes significantly to perinatal and maternal mortality and morbidity. Some non-modifiable risk factors of PIH are family history of PIH, extremes of reproductive age, hypertension in previous pregnancy, DBP >80 mmHg at 1st visit, multiple pregnancy,

underlying chronic illnesses like diabetes mellitus, hypertension and renal diseases. Modifiable risk factors include BMI >35 Kg/m.^{2,3}

Though the mechanism of genesis of PIH isn't known, it is proposed to be due to an excessive inflammatory response in the mother secondary to placental or maternal factors.⁴ Research studies revealed a positive association between oxidative stress and PIH which is thought to be the underlying pathophysiology. Both exaggerated inflammation and oxidative stress can lead to altered endothelial function and increase in coagulability. The interplay among oxidative stress, inflammation, endothelial dysfunction and the hypercoagulable state results in the PIH development.⁵ All of these factors are known to cause elevated sympathetic activity, which is a sign of autonomic dysfunction. Irrespective of contributing factors, sympathetic overactivity results in sustained vasoconstriction, which is the major pathophysiologic mechanism of PIH.⁶ Similar studies have reported significantly reduced HRV among pregnancy-induced hypertension women when compared with normotensive pregnant women.⁷

From this, we hypothesize that the women with risk factors for developing PIH, are prone to an increased state of oxidative stress and inflammation that can potentiate the genesis of PIH in later trimester of pregnancy and pose as a cardiovascular (CV) risk. Studies have reported that autonomic dysfunction is a depiction of the underlying CV risk. Short-term HRV analysis, is the non-invasive and reproducible marker of cardiovascular autonomic modulation.⁸ The study objective was to measure the magnitude of sympathovagal imbalance (SVI) and to evaluate the relationship between inflammatory response and oxidative stress in the genesis of sympathovagal imbalance in pregnant women with risk factors for pregnancy induced hypertension.

METHODS

Study setting and study period

After enrolling subjects from JIPMER (Jawaharlal Institute of Post Graduate Medical Education and Research), Obstetrics and Gynaecology Department, Puducherry, South India, a cross-sectional study was conducted at the Department of Physiology between March 2023 and February 2024.

Study population

Patients with any of the following medical illnesses such as chronic diabetes mellitus, chronic hypertension, renal diseases, early or late pregnancy, DBP at first-visit of ≥ 80 mm Hg, and frequent pregnancies, and BMI >35 kg/m² were included as cases in the study. Additionally, pregnant women with a family history of PIH and PIH in previous pregnancies were included. Pregnant women

who were age-matched, normally healthy, and free of known risk factors for PIH served as the controls. The study participants excluded were those diagnosed with cardiac arrhythmias, usage of oral contraceptives prior to pregnancy, and unclear last menstrual date.

Sample size

Based on prevalence of autonomic dysfunction among women with pregnancy induced hypertension,⁹ the sample size was determined to be 80, with 6% relative error, a 95% confidence interval and 20% expected non-response rate. The Obstetrics and Gynaecology department at the hospital used sequential sampling as the sampling technique. Individuals with acute abdomen who fulfilled the study's inclusion requirements and expressed willingness to take part were added one after the other.

Procedure

Upon obtaining written informed permission in the vernacular language of the area, study participants who fulfilled the eligibility requirements were admitted into the research. It was instructed to the study participants to fast overnight and wear loose clothing when they reported to the autonomic function testing facility.

A 12-hour coffee-free period was instructed to them before the test. Anticholinergics, antihistamines, diuretics, over-the-counter cough and cold remedies, sympathomimetics and parasympathomimetic drugs were among the drugs that study participants were advised to avoid using for 48 hours before the trial. It was recommended that they stop using long-acting antagonists 48 hours prior to the test and short-acting α and β antagonists 24 hours beforehand. The test was postponed in the event that the subjects experienced any health problems that led to poor quality sleep the previous night or prodromal symptoms such as fever and body ache. The study participants were advised to evacuate bowel and bladder prior to the test.

Anthropometric measurements and Short-term Heart Rate Variability (HRV) and basal parameters of cardiovascular system were recorded. Blood samples were collected for analysis by following the below described procedures. Both the weight and the height were recorded. In order to prevent zero and parallax errors, a spring balance was utilized to measure weight to the nearest half kilogram and a wall-mounted stadiometer was employed to measure height to the nearest millimetre.

Basal cardiovascular parameters and short-term HRV

For a duration of five to ten minutes, the study participants were instructed to lie comfortably in the left lateral position on a couch. They were told in their own language about the surgery, which helped to allay their anxieties. The proper transducers were connected in order to monitor lead II of the ECG (Electrocardiogram). Using

Acknowledge 3.8.2 software and the Powerlab 8/30 ML 870 data acquisition apparatus, the data was collected at a rate of 500 samples/second for every channel.

The oscillometric method was used to evaluate the heart rate and stable baseline supine blood pressure using Omron MX3 automated blood pressure monitor from India. After that, for the next five minutes when the patient was at complete rest, the lead II ECG was obtained for short-term HRV study. After an overnight fast of 12 hours, six millilitres of venous blood were drawn in an aseptic manner for biochemical analysis.

Parameters used in the study

(i) BMI was computed using the Quetelet's index which is calculated by $\text{Weight}/(\text{Height})^2$ (Height measured in meters, Weight in kilograms)

(ii) The RPP or Rate Pressure Product is $(\text{SBP} \times \text{HR})/100$, where SBP is Systolic Blood Pressure and HR is Heart Rate

(iii) HRV Analysis: After using bandpass filters to extract the 5-minute resting (lead II) ECG, it was meticulously inspected for artifacts, ectopics and they were removed manually then. R waves were found using thresholding method in acknowledge software. Next, the text format of the recording was used to extend the RR tachogram. Frequency and temporal domain measurements were obtained from the RR tachogram using HRV analysis software (Biosignal analysis group, version 1.1 Finland). The quick Fourier transform was utilized to compute heart rate power spectra. Low Frequency (LF) and High Frequency (HF) components (both ms^2 and nu), power (ms^2), and the LF-HF ratio were studied in the frequency domain. Statistical indicators including RR interval (ms), Standard Deviation of Normal-to-Normal interval (SDNN) (ms), Square root of the Mean Squared Differences of Successive normal to normal intervals (RMSSD) (ms), the number of interval differences of successive NN intervals greater than 50 ms (NN50), the proportion derived by dividing NN50 by the total number of NN intervals (pNN50) were studied in the time domain indices,

(iv) Biochemical Parameters: The following biochemical parameters were assessed using an automated analyser and diagnostic kit from Accucare Lab Care. Enzymatic colorimetric technique for medical diagnosis: 150-250 mg/dl is the normal range for total cholesterol (TC); 45-60 mg/dl for high-density lipoprotein (HDL); 65-165 mg/dl for triglycerides (TG); 45-60 mg/dl for Very Low-Density Lipoprotein (VLDL), or low-density lipoprotein (LDL) and $\text{LDL} = \text{TC} - \text{HDL} - \text{TG}/5$ for LDL. VLDL-C and LDL was established by the Friedwald formula ($\text{VLDL} = \text{TG}/5$ and $\text{LDL} = \text{TC} - \text{HDL} - \text{TL}/5$). An enzyme immunoassay method was used to measure High-sensitivity C-

reactive protein (hs-CRP) and leptin using a diagnostic kit from DBC Diagnostic Biochem Canada Inc. In lean women, the typical range for leptin is 3.7-11.1 ng/ml. An enzyme immunoassay was done with the diagnostic kit for Tumor Necrosis Factor-alpha (TNF- α) from Ani Biotec Oy, Origenium Laboratories Business Unit. The lipid risk ratios that follow were calculated: LDL/HDL, TC/HDL, TG/HDL, and Atherogenic index as $\text{Log}(\text{TG}/\text{HDL})$. Malondialdehyde (MDA) lipid peroxidation was examined using a colorimetric method with the help of Cayman's TBARS assay kit. (Normal range: MDA - 1.86 to 3.94 μM). Using a colorimetric method, the Cayman's Antioxidant Assay was utilized to assess the overall state of antioxidants (Typical range: 0.5-2 μM).

Statistical analysis

All collected data were put into Excel spreadsheet in Microsoft Office before being imported in IBM SPSS version 21.0 for analysis. To test normalcy of the data, Kolmogorov-Smirnov test was used to evaluate. The Unpaired Student's T-test and Mann-Whitney test were used to look at the mean differences between controls and cases. The relationship of the LF-HF ratio with (Basal Heart Rate) BHR, metabolic parameters, Blood Pressure (BP) and Alpha-Fetoprotein (AFT) parameters were examined using Spearman's correlation test and Pearson correlation analysis. If the probability of chance was less than 0.05, the difference was considered significant statistically ($p < 0.05$).

RESULTS

Forty pregnant women with PIH risk factors were recruited and compared to forty pregnant women who were age-matched and in good health.

The study groups' baseline characteristics

The cases and controls were found to belong to the same mean age group when comparing the age, anthropometric, and basal cardiovascular characteristics ($p = 0.1412$). Among the forty pregnant women with PIH risk factors, the BMI was considerably higher ($p = 0.0252$). When comparing the patients to controls, there is a significant increase in the baseline cardiovascular measures, including HR, SBP, DBP, MAP, and RPP ($p < 0.0005$), (Table 1).

Short term HRV analysis

Frequency domain parameters

When frequency domain parameters of short-term HRV were analysed, it was shown that the cases had significantly lower total power (TP) ($p = 0.0048$), which was accompanied by lower LF and HF power ($p < 0.0001$). In comparison with the controls, there was a 33.9% decrease in TP in the patients. In compared to controls, cases showed a substantially raised LF nu ($p = 0.0306$)

and depressed HF nu ($p = 0.0308$). The absolute powers were reported in normalized units. Compared to controls, the HF nu in cases was 12.83% lower while the LF nu was 16.1% higher in cases. In comparison to the LF power drop in cases (7%), the HF reduction in instances

(16.65%) was greater. “LF-HF” ratio, which was considerably higher among cases ($p = 0.0229$), also showed this. It was discovered that “LF-HF” ratio in patients was 40.08% greater than in the controls.

Table 1: Comparing baseline attributes of controls and cases, (n = 80).

Parameters	Controls (n = 40), Mean±SD	Cases (n = 40), mean±SD	P value
Age (years)	25.15±2.39	26.3±4.27	0.1412
BMI (Kg/m ²)	22.18±3.26	24.34±5.021	0.0252*
HR (per min)	84.05±10.42	92.38±6.33	0.0001*
SBP (mm Hg)	101.23±7.58	107.68±9.97	0.0017*
DBP (mm Hg)	61.58±5.86	68.20±3.59	0.0001*
MAP (mm Hg)	74.79±5.87	81.36±4.67	0.0001*
RPP (Bpm. mm Hg)	85.37±14.14	99.46±11.45	0.0001*

Unpaired student's T-test done. *Significant p-value; BMI: Body Mass Index; HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; RPP: Rate Pressure Product

Table 2: Comparing time domain basal cardiovascular parameters and frequency among controls and cases, (n=80).

Parameters	Controls (n=40), mean±SD	Cases (n=40), mean±SD	P value
Frequency domain			
TP (ms ²)	306.15±151.42	202.35±167.73	0.0048*
LFnu	44.34±15.46	51.49±13.51	0.0306*
HFnu	55.66±15.46	48.52±13.51	0.0308*
LF (ms ²)	98.00±57.76	52.0±29.91	0.0001*
HF (ms ²)	167.3±96.8	78.13±70.56	0.0001*
LF-HF ratio	0.785±0.418	1.10±0.75	0.0229*
Time domain indices			
Mean RR(s)	0.714±0.098	0.644±0.07	0.5384
SDNN(s)	26.73±11.97	23.00±8.16	0.0680
RMSSD (ms)	27.48±19.69	22.6±10.01	0.1663
NN50	46.08±69.08	13.18±16.92	0.0045*
pNN50	12.15±18.04	5.21±7.28	0.0269*
RR index	0.05±0.018	0.05±0.02	0.9999
TINN	143.3±93.55	118.63±41.97	0.1321

Unpaired student's t test done. *Significant p-value; TP : Total Power; LF : Low Frequency component; LF nu : LF component expressed as normalized unit; HF : High Frequency component; HF nu: HF component expressed as normalized unit (HF nu); SDNN : Standard Deviation of Normal to Normal interval; RMSSD : Square root of the mean squared differences of successive normal to normal intervals; NN50 : the number of interval differences of successive NN intervals greater than 50 ms; pNN50 : the proportion derived by dividing NN50 by the total number of NN intervals. TINN: The triangular interpolation of NN interval histogram

Time domain parameters

When comparing patients to controls, the mean RR interval decreased by 9.8%, according to the time domain parameter analysis but this difference wasn't significant statistically. NN50 ($p = 0.0045$) and pNN50 ($p = 0.0269$) among patients exhibited a drastic decline. Just 57.12% of the pNN50 found in controls was present in the cases, (Table 2).

Biochemical parameters, inflammatory and oxidative stress markers

Between the instances, TG and VLDL were considerably greater ($p=0.0102$ and $p=0.0101$). On comparing with controls, there was a drastic difference in HDL, LDL,

TC, and TC/HDL, however HDL was lower and LDL was greater among cases. TG/HDL and atherogenic index, two lipid risk ratios, were substantially elevated in cases ($p=0.0180$ and $p=0.0240$). When comparing patients to controls, it was discovered that TNF- α , hs-CRP, and leptin were considerably higher in cases ($p<0.0001$). Serum MDA levels demonstrated a considerable increase in lipid peroxidation among cases on comparing with controls ($p = 0.0048$), while the total antioxidant capacity was declined significantly among cases ($p<0.0001$), (Table 3).

Correlation analysis

The current investigation demonstrates a robust link between LF-HF ratio and inflammatory cytokines like

TNF- α ($r = 0.812$, $P < 0.001$) and hs-CRP ($r = 0.945$, $P < 0.001$), hence endorsing the hypothesis that patients with PIH risk factors also exhibit inflammation and sympathovagal imbalance. In the present investigation, there is a strong negative connection ($r = -0.420$, $P = 0.007$)

between the LF-HF ratio and total antioxidant capacity and substantial positive association ($r = 0.828$, $P < 0.001$) between MDA and LF-HF. The atherogenic index and leptin levels do not significantly correlate with LF-HF ratio in current investigation, (Table 4).

Table 3: Comparing lipid profile and lipid risk factors parameters between controls and cases, (n=80).

Parameters	Controls (n=40), mean $\pm$ SD	Cases (n=40), mean $\pm$ SD	P value
TC (mg/dL)	185.5 $\pm$ 19.74	200.20 $\pm$ 42.59	0.0512
TG (mg/dL)	164.80 $\pm$ 45.06	194.48 $\pm$ 55.24	0.0102*
HDL (mg/dL)	58.53 $\pm$ 13.93	56.20 $\pm$ 14.32	0.4630
LDL (mg/dL)	93.99 $\pm$ 19.99	105.11 $\pm$ 38.50	0.1090
VLDL (mg/dL)	32.96 $\pm$ 9.01	38.90 $\pm$ 11.05	0.0101*
TC/HDL	3.33 $\pm$ 0.85	3.72 $\pm$ 0.96	0.0580
TG/HDL	2.95 $\pm$ 1.07	3.79 $\pm$ 1.92	0.0180*
LDL/HDL	1.74 $\pm$ 0.72	1.96 $\pm$ 0.81	0.2030
AI	0.47 $\pm$ 0.03	0.54 $\pm$ 0.19	0.0240*
MDA (μ M)	2.11 $\pm$ 0.57	2.86 $\pm$ 0.89	0.0048*
TAOS (mM)	0.766 $\pm$ 0.185	0.508 $\pm$ 0.271	0.0001*
Human TNF- α (pg/mL)	18.22 $\pm$ 7.96	26.34 $\pm$ 8.68	0.0001*
Leptin (ng/mL)	12.31 $\pm$ 6.85	20.37 $\pm$ 9.48	0.0001*
hs-CRP (mg/L)	3.88 $\pm$ 0.62	9.43 $\pm$ 2.45	0.0001*

Unpaired student's t test was applied. *Significant p-value; TC: Total Cholesterol; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; VLDL -C: Very Low-Density Lipoprotein; TG: Triglycerides; AI: Atherogenic Index; MDA: Malondialdehyde; TAOS: Total antioxidant status; TNF- α : Tumor Necrosis Factor- α ; hs-CRP: High Sensitivity C-Reactive Protein

Table 4: Correlating LF-HF ratio with biochemical parameters among cases and controls, (n=80).

Parameters	Cases (n=40)		Controls (n=40)	
	r	p	r	p
TNF- α (pg/mL)	0.812	0.001*	0.154	0.344
hs-CRP (ng/mL)	0.945	0.001*	0.044	0.786
Leptin (ng/mL)	0.065	0.692	0.094	0.563
MDA (μ M)	0.828	0.001*	0.161	0.321
TAOS (mM)	-0.420	0.007*	0.123	0.450
AI	0.075	0.647	0.112	0.491

*Significant p-value; TNF- α : Tumor Necrosis Factor- α ; hs-CRP: High Sensitivity C-Reactive Protein; MDA: Malondialdehyde; TAOS: Total antioxidant status; AI: Atherogenic Index

DISCUSSION

Our study observations reveal that there is significant elevation of cardiac parameters i.e. HR, SBP and DBP increased resting HR in cases might be linked to a drop in vagal activity. Also, sympathetic overactivity could contribute to an elevated HR.¹⁰ The elevated levels of DBP and SBP observed in certain situations may be attributed to an increased adrenergic drive, given that sympathetic modulation primarily governs blood pressure regulation.¹¹ This was consistent with earlier studies which revealed the higher BHR, SBP and DBP in pregnant women with risk factors of PIH in all pregnancy trimesters, which might be attributed to the increase in sympathetic tone as PIH is first and foremost a state of sympathetic overactivity.⁶ It was also observed that RPP and MAP were also higher significantly among cases when compared to controls. RPP, an index of myocardial oxygen demand is higher among the cases indicating the

higher cardiovascular risk among the pregnant women with risk factors.¹²

The increase in sympathetic tone can be further corroborated with findings in analysis of short-term HRV. The frequency domain parameters showed a considerable reduction in the TP index of the overall magnitude of HRV in the patients. Additionally, a notable distinction was observed in the percentage contribution of the parasympathetic (HF power) and sympathetic (LF power) components between the cases and controls, indicating the type of autonomic imbalance that existed in the cases. The LF-HF ratio was significantly higher in cases when comparing with the controls. The increased LF-HF ratio represents decreased parasympathetic and increased sympathetic drives to heart.⁸ This was further evidenced from increased LFnu and decreased HF and HFnu. The decrease in LF power is attributed to grossly reduced power of HRV spectrum. The sympathovagal

balance was evidenced to be deviated more towards the adrenergic system in cases. A similar kind of observation was derived from normalization of absolute powers in the form an increased LFnu and lowered HFnu. The LFnu in cases was 16.1% higher and HF nu was 12.83% lower in cases in comparison to controls. The reduction in HF in cases was more when compared to the reduction in LF power in cases. Previous research demonstrated that vagal withdrawal (at least in early stages of PIH) also led to sympathovagal imbalance. This is because HFnu, which indicates vagal regulation of SA nodal discharge, was lower in PIH patients than in control group during 12th week of recording.⁸ In the present study, this was also reflected in the LF-HF ratio, sympathovagal balance marker was significantly elevated among cases. The LF-HF ratio among cases was 40.08% elevated than the controls.

The analysis of the time domain parameters demonstrated a drop in mean RR interval. The reduction observed in the mean RR interval was 9.8% but wasn't significant statistically. Significant decrease was found in NN50 and pNN50 among cases. The pNN50 observed in cases was only 57.12% of that seen in controls. The high frequency variations in the short-term ECG recording are represented by these time domain indices. The decline in the parameters indicates a lower level of vagal regulation of cardiac activities, which is in line with the results of frequency domain analysis.

Therefore, in cases with risk factors for PIH, there is a substantial change in autonomic regulation, manifested as a decreased HRV with increase in sympathetic drive and subdued parasympathetic activity during supine rest. Decreased TP of HRV has been reported as a significant cardiovascular risk factor. Also, a decreased parasympathetic and an increased sympathetic modulation have been reported as poor CVS health markers as evident from studies on myocardial infarction patients.⁸ The increased resting BP and HR has been postulated as independent CVS risk factors.^{10,11} It is clear from our research that the study group possesses each of the risk factors listed above, which could endanger their cardiovascular health.

Pregnant women with risk factors of PIH have a constellation of factors which can tax the autonomic system and cause this alteration in the autonomic modulation in them. In the present study, inflammatory cytokines levels of TNF- α and hs-CRP were found to be significantly increased in cases when comparing with controls in the early part of mid-trimester. Earlier studies support the evidence of increased hs-CRP and TNF- α levels in preeclampsia patients but there are conflicting reports to demonstrate increase in TNF- α and hs-CRP in early part of pregnancy.¹³

In the current study, there is strong association of LF-HF ratio with inflammatory cytokines like TNF- α and hs-CRP which supports the association of inflammation and

sympathovagal imbalance in patients with PIH risk factors. Given reports that cytokines released peripherally cross the blood-brain barrier and influence activities of various brain centres, researchers have hypothesized that the so-called placental factors may be acting primarily on medullary cardiovascular centres in the brain to modulate central parasympathetic outflow rather than only acting peripherally on the blood vessels to alter vascular tone.¹⁴

Lipid peroxidation as evidenced by serum levels of MDA was significant statistically among cases when compared to controls and total antioxidant capacity was significantly lower in cases. Studies have showed increased lipid peroxidation levels in preeclampsia.¹⁵ Results of the present study demonstrate increased lipid peroxidation in pregnant women with PIH risk factors from the early mid-trimester compared to the normal age-matched, parity-matched pregnant women without this risk factors.

In the current study, we also obtained a significant positive association of MDA with LF-HF ratio and significant negative correlation of total antioxidant capacity with LF-HF ratio supporting the association of oxidative-antioxidative status and sympathovagal imbalance in patients with risk factors of PIH. Research has demonstrated that the rise in sympathetic output that occurs prior to the onset of hypertension is mediated by oxidative stress in the central nervous system.¹⁶

Leptin was found to be increased significantly in cases when comparing with the controls. Studies have reported increased leptin level in preeclampsia.^{17,18} Renal sympathetic activation in response to leptin was expected to elevate blood pressure.¹⁹ However, in the current study, there isn't significant correlation of leptin levels with LF-HF ratio.

Total cholesterol, Very Low-Density Lipoproteins (VLDL), triglycerides were higher significantly among the cases compared with controls. HDL and VLDL didn't show significant difference between two groups but HDL was decreased in cases and LDL was higher among cases when compared to controls. The lipid risk ratios atherogenic index and TG/HDL were higher significantly among the cases indicating the higher cardiovascular risk among cases. According to studies, oxidized lipids can cause endothelial dysfunction either directly or indirectly through effects on prostaglandins, such as an increase in thromboxane synthesis and an inhibition of prostacyclin synthesis. This can cause patients who have PIH risk factors to develop PIH.^{5,20,21} Studies have also revealed that autonomic imbalance, inflammation and dyslipidaemia are closely interlinked, each factor promoting the development of the other.^{22,23}

Further, these subjects had CV risks in the form of decreased TP of HRV, increased RPP and increased atherogenic index. Moreover, PIH has a significant adverse impact on maternal and foetal health. Autonomic

dysfunction could be an early marker of the development of PIH in this high-risk group of pregnant women. If diagnosed early, it may enable an early intervention in preventing the development of PIH and its complications. This would help in providing a better cardiovascular and reproductive health to the expectant mothers with risk factors of PIH.

There were few limitations of the study. Bodyfat percentage was not measured in this study. Assessment of body fat percentage would have been much more specific index of adiposity than BMI. CAFTs should have been performed to assess autonomic reactivities to various stimuli.

CONCLUSION

Based on findings observed in current study, we conclude that pregnant women with risk factors of PIH have a derangement in autonomic function in the form of attenuated heart rate variability and reduced parasympathetic activity & increased sympathetic activity from their early mid-trimester of pregnancy. Pregnant women identified with risk factors for pregnancy induced hypertension showed the presence of significant co-morbid factors in the form of increased inflammatory response, oxidative stress and dyslipidaemia compared to the age-matched normal pregnant women. Autonomic imbalance resulting from the interplay of these co-morbid factors could predispose to CV risks and future CV morbidities. Hence, conducting sessions for stress management not only during pregnancy but also in the pre-pregnancy period can alleviate sympathetic dysfunction. Educating family members for healthy family environment during pregnancy.

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Ethical approval: The study was approved by the Institutional Ethics Committee for Observational Studies, JIPMER, Puducherry

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