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Research Paper

A Study of Non-Linear Heart Rate Variability in Pregnancy In Rural Indian Women

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***ABSTRACT**:*
Objective: *The objective of the study was to investigate the adaptation of autonomic control during pregnancy based on non-linear heart rate variability analysis.*
Methods: *Twenty-five normal healthy volunteer women and 22 pregnant women from rural area(32 to 38 weeks of gestation) underwent various analyses of HRV following a standard sampling. Time domain and frequency domain measures as well as non linear analysis parameters of HRV were compared between same pregnant women in first and third trimester by paired Student's t-test as well as with non pregnant women as controls by unpaired Student's t-test. various analyses of heart rate variability following a standard sampling.*
Results: *Time domain, frequency domain and even non linear parameters of HRV showed no statistically significant differences in control group and pregnant women during first trimester. Comparison between control group and pregnant women in third trimester showed pregnant patients had higher heart rates, and decreases in some time domain heart rate variability parameters. High frequency (HF) power decreased statistically significantly (p<0.05) in pregnant women with increase in LF%, LF/HF ratio as well as LF nu (normalized units) (p<0.05). statistically significant alterations in absolute High Frequency (HF) power, Root of Mean Squared Standard Deviation (RMSSD) of RR intervals and some non linear parameters like Standard Deviation 1 (SD1) and correlation dimension D2, whereas almost all the parameters both linear and non linear showed statistically significant differences with progression of pregnancy from first to third trimester.*
Conclusion: *Results suggest that normal pregnancy is associated with a facilitation of sympathetic regulation and decrease in parasympathetic influence on ANS. Decrease in non linear HRV parameters suggested decreased complexity of the autonomic control system. Non linear HRV parameters were altered to a larger extent than linear HRV parameters suggesting Further longitudinal studies with large sample size are needed to generate normative data of linear and non linear HRV parameters in pregnancy.*
***Keywords**: Autonomic function, Heart rate variability, Pregnancy*

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I. INTRODUCTION :

In the field of gynecology, HRV is especially suitable for pregnant women because it is virtually noninvasive and produces the least stress on mother and infant. Adaptation of cardiovascular system to changing hemodynamic needs during pregnancy requires a well-controlled interaction between sympathetic and parasympathetic system [1].). Because it is still not clear whether normal pregnancy coincides with alternations in the autonomic functions, we applied the standard method of short-term HRV analysis((2, 10) to evaluate theANS functions in normal pregnancy and non pregnant women. This study tests the hypothesis that HRV analysis is capable of detecting the changes in sympathetic and parasympathetic controls of heart rate in normal pregnancies and control .Non linear system analysis of HRV [3] has advantages over traditional time and frequency domain techniques as it measures the functional order and temporal unfolding of heart rate [4] by treating heart rate as an information generating source. It detects high-risk, abrupt autonomic changes better than conventional techniques [5,6]. Non linear methods better quantify the chaotic dynamics of HRV. However, non linear HRV parameters are not being studied may be due to complex statistical methods and non inclusion of these parameters in most of the HRV software in use. HRV data in Indian rural pregnant women is very meagre [7-8]. Moreover, non linear HRV studies are not found in literature for Indian pregnant women though non linear HRV has been studied in pregnant women in some other population [9]. The aim of the current study was to study ANS adjustments during pregnancy by means of linear as well as non linear HRV analysis by a longitudinal study and to compare these analyses with HRV analyses of non pregnant women.

II. MATERIALS AND METHODS

A prospective cohort study was conducted for studying autonomic function responses during progress of pregnancy in third trimester. Also, the comparison of autonomic functions in pregnant and non pregnant females was done, making it a case-control study. Study duration was two years from January 2008 to December 2010. The study protocol was approved by the Institutional Ethics Committee and study was performed in accordance with the ethical standards as laid down in the 1964 declaration of Helsinki and its later amendments.

Study group were enrolled from Department of Obstetrics & gynaecology from Acharya Vinoba Bhave Rural Hospital (AVBRH) attached to a Jawahar Lal Nehru Medical college (JNMC) Sawangi (Meghe) Wardha. Inclusion criteria for study group were pregnant females (age range of 24-30 years) of 32 to 34 weeks of gestation with parity 1 with single normotensive pregnancy, normal findings on physical examination, ECG, and routine blood tests including Hb% and blood sugar. Females with history, signs, or symptoms of cardiovascular, pulmonary, or endocrine diseases as assessed by detailed history taking and thorough clinical examination were excluded from the study.

Study participants were explained about the detailed plan of work and aim of the present research work. Written informed consent was obtained from all individual participants included in the study. HRV was measured in third trimester of pregnancy during 32-34 weeks of pregnancy. Those who dropped out of study were not included in the final analysis. Those who were diagnosed by obstetricians as having pregnancy induced hypertension later were also excluded.

Considering possible attrition and exclusion criteria for women who turned hypertensive during follow-up, total 32 women were studied, out of which 8 could not be followed up for assessment in third trimester and 2 turned hypertensive in third trimester, who were excluded from the study group. Thus, study group comprised of 22 pregnant women. Twenty five healthy non pregnant subjects of the same age group were selected in the control group from amongst the healthy relatives of the study participants so as to match the socioeconomic status with similar inclusion criteria except pregnancy.

Resting Supine Electrocardiogram (ECG) recordings for 10 minutes were obtained for all subjects in the same quiet room after the subject had 20 minutes of rest in supine position. The recordings were made between 10:00 am and 12:00 noon to obviate diurnal influences. ECG was recorded continuously on a computerised data acquisition and analysis system (Powerlab, AD Instruments).

The analogue to digital conversion of the ECG signal was done .using A/D converter with the sampling frequency 5 kHz. In order to avoid interference of any artefacts, the ECG recordings and the corresponding event series were manually checked for artefacts and only artefact-free sections were included in analysis. RR text files (all RR intervals in milliseconds in a text file format) were generated with Lab Chart Pro and further HRV analysis i.e., frequency and time domain analysis and non linear analysis was done using HRV analysis software of Kubios HRV version 2.2.

For frequency domain analysis, fast fourier transformation was done using window width of 256 seconds and Window overlap of 50%. Entire spectrum of frequencies was divided into three major bands, very low frequency (VLF, 0-0.04 Hz), low frequency (LF, 0.04-0.15 Hz) and high frequency (HF, 0.15-0.4 Hz). For computing HRV indices during supine rest, recommendations of the task force on HRV were followed [10].

STATISTICAL ANALYSIS

Descriptive statistics like mean and standard error of mean was used to describe linear and non linear HRV parameters in both the groups. Normality of the data was tested by Lilliefors test. As data distribution was normal for all parameters under consideration, Student's t-test was applied for between groups comparison. Paired t-test was used for comparison between first trimester and third trimester evaluation. Unpaired t-test was used for comparison between pregnant women and control group. Comparisons were made using two-tailed significance at probability less than 0.05.

III. RESULTS

As age is the confounding factor for HRV analyses, two groups were analysed and were found to be similar for age (Mean age±SD – control group 23.71±2.75 years, study group 23.16±2.28 years; t-test, $p>0.05$). Results of HRV parameters (both time domain and frequency domain) in pregnant and non pregnant groups for linear HRV and non linear HRV are shown in graphs(Figure No. 1- 14) respectively . where as comparison of linear and non linear HRV analysis in different groups is given in [Table/Fig-1,2] respectively.

Time domain, frequency domain and even non linear parameters of HRV Comparison between control group and pregnant women in third trimester showed statistically significant alterations in absolute HF power, RMSSD and some non linear parameters like SD1 and correlation dimension D2, whereas almost all the parameters both linear and non linear showed statistically significant differences between nonpregnant and pregnant group respectively.

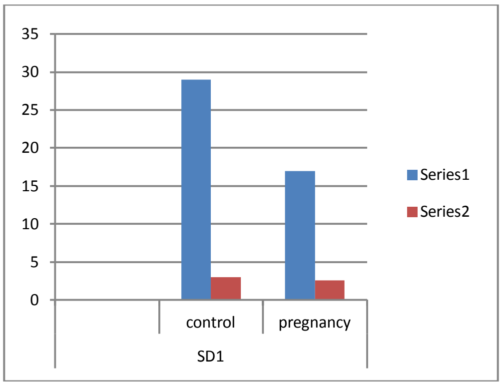
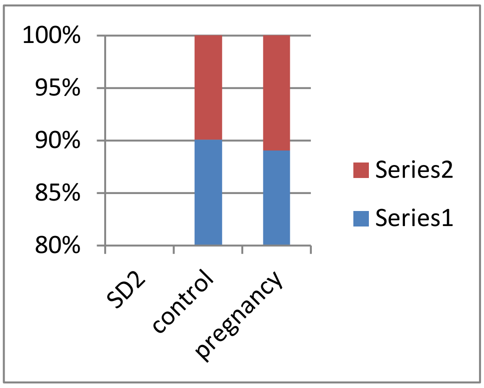


Figure 1



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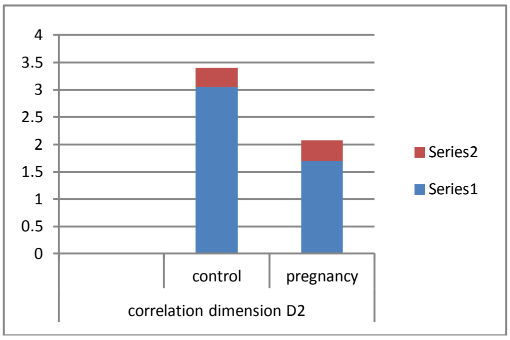

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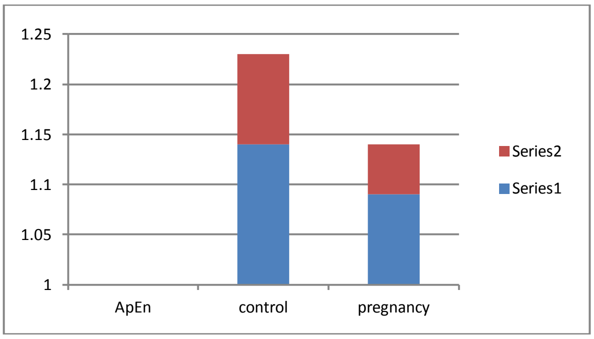

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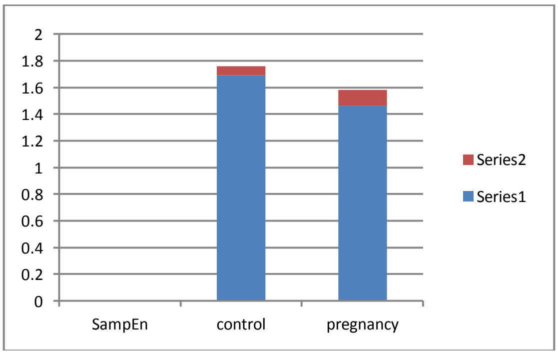

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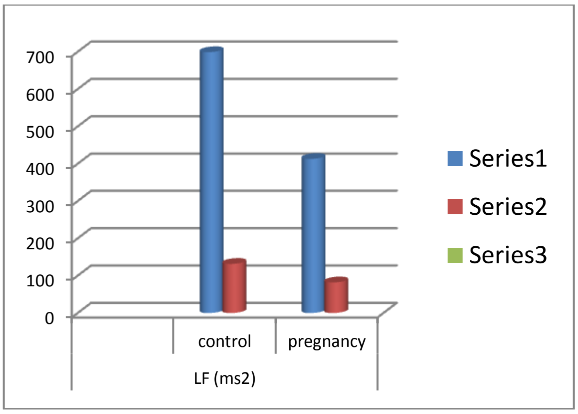

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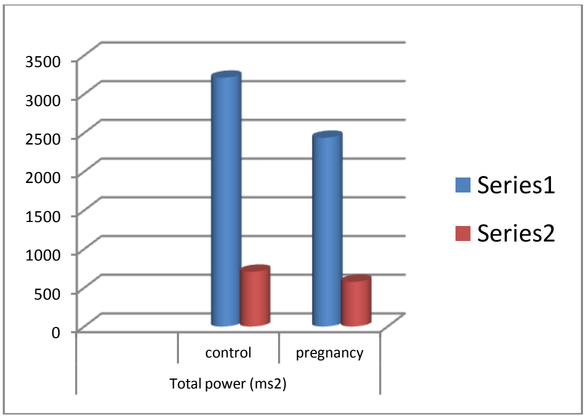

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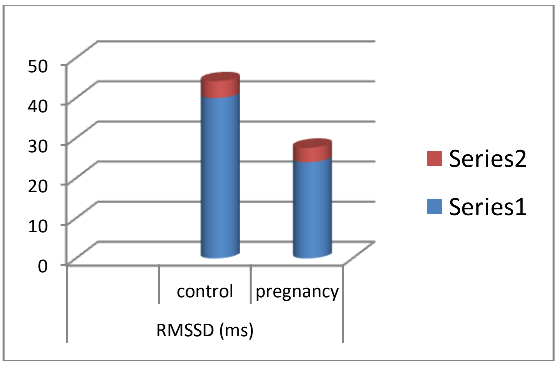

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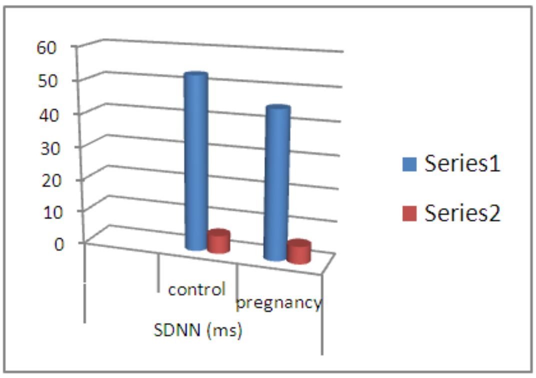

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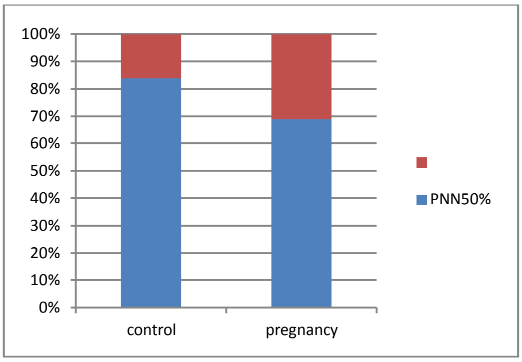

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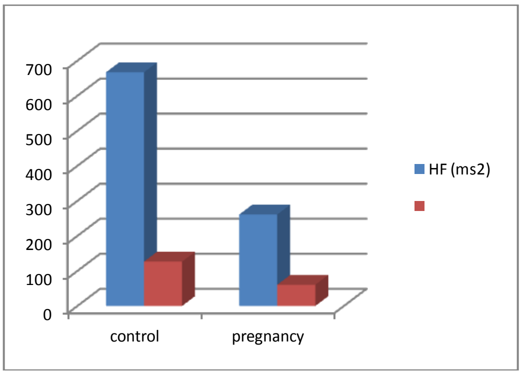

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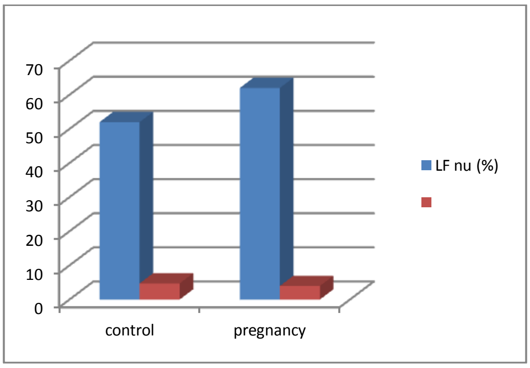

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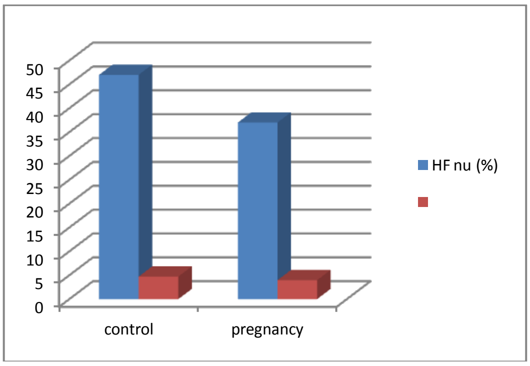

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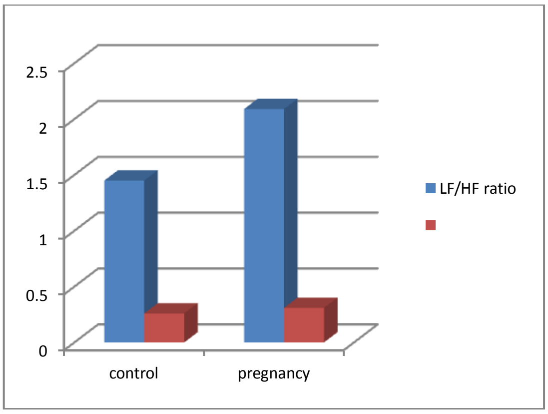

Figure 14

Table No.1 : Comparison of time domain and Frequency domain HRV parameters in different groups.** highly signifiant (p<0.01), *** Very highly signifiant

Parameter	non pregnant vs. third trimester(Unpaired t-test)
Total power (ms2)	**t=0.849 p=0.403**
SDNN (ms)	**t=0.991 p=0.330**
RMSSD (ms)	**t=2.917 p=0.007****
PNN 50 (%)	**t=2.670 p=0.013**
HF (ms2)	**t=2.89 p=0.009****
LF (ms2)	**t=1.844 p=0.078**
LFnu (%)	**t=-1.622 p=0.117**
HF nu (%)	**t=1.622 p=0.117**
LF/HF ratio	**t=-1.544 p=0.134**

Table No .2: Comparison of non linear HRV parameters in different groups.
*** signifiant (p<0.05), ** highly signifiant (p<0.01), *** Very highly signifiant (p<0.001)1)**

Parameter	non pregnant vs. Third trimester (Unpaired t-test)
SD1	t=2.928 p=0.007**
SD2	t=0.697 p=0.491
Correlation Dimension D2	t=2.619 p=0.014*
ApEn	t=0.461 p=0.649
SampleEn	t=1.549 p=0.136

IV. DISCUSSION :

Pregnancy is a state where multiple physiological readjustments are required for the growth of embryo, perhaps affecting cardiovascular system the most.[11] The profile of cardiovascular parameter changes, and it is varied compared to non-pregnant state it advances.[12] Cardiac dysautonomia can be seen when females fail to adapt increased demand and cardiovascular readjustment.[13] This can be seen in the form of reduced vagal tone and/or increased sympathetic tone that manifest as reduced heart rate variability.[14] We explored whether it is reduced significantly in normal pregnancy too. We found, in general, reduced heart rate variability in pregnant females than controls. Though frequency domain revealed stronger differences than time-domain HRV parameters, our results are in line with previous HRV studies done with reference to normal pregnancy which have reported the same finding.[12,14-17] This can be due the fact that time-domain analysis needs 24 h HRV,[18] and we used only 5 min HRV. Apart from pregnancy itself, other factors contributing to reduced HRV in this study can be: 1) higher BMI (27 kg/m2), 2) middle to upper socio economic class rather than lower, 3) presence of primipara (two-third), 4) low mean haemoglobin level (mean 11 gm%), 5) urban life style, 6) dietary salt intake, and 7) subjective apprehension of procedure.

Two recent studies are noteworthy here. One study[17] compared HRV in pregnancy indicating reduced HRV in first as compared to third trimester indicating that sympathovagal imbalance and abnormally low HRV are more pronounced using the later stage of normal pregnancy. However, here we have taken all subjects with previous good obstetric and reproductive history and matched controls to compare with. So even first trimester HRVs showed significant lowering as compared to non-pregnant controls. In another study,[19] the same sympathovagal imbalance was found altered but with the use of other autonomic function testing than HRV in the third trimester of pregnancy. We included all three trimesters and despite overall reduced HRV, could not find any trimester of three as dominant for major change. In general, second and third trimester showed decline as compared to first trimester. But in post hoc test analysis there was no significant inter-trimester difference of HRV, indicating that cardiac autonomic change ensues in pregnant female from first trimester and it can accumulate to culminate in some aftermaths like arrhythmia and hypertension with months of amenorrhoea to come. However, it needs follow up study on the same gravid subjects from first trimester to ascertain it further. A similar study done similarly has shown that reduced HRV indicates either increased sympathetic activity or reduce vagal activity or both.[20] Altered LF/HF ratio indicates the same cardiac dysautonomia. Normal value of this ratio is 1.5-2,[20] but cases had low ratio indicating alteration in cardio vagal balance. Even in controls we found this ratio low than this range and that indicates sympathetic over activity in young non-gravid females. Similarly, SD1:SD2 ratio based on HRV geometric analysis was reduced that shows sympathetic over activity in gravid subjects.[21] Raised heart rate with significance difference also indicated sympathetic overdrive. Pregnancy requires cardiac adjustments which are mediated by change in cardiac autonomic balance towards sympathetic than normal vagal influence. However, excess of sympathetic activity and reduced HRV indicates that heart is under physiological stress. This stress can lead to preeclampsia and pregnancy induced hypertension which adversely affects the overall outcome and proceedings of pregnancy which is otherwise a physiological adaptation.[22] Parity is one of the factor affecting cardiac autonomic balance and alteration in pregnancy. Primipara with the first exposure to need of cardiorespiaritory adjustment is more at risk for the cardiac dysautonomia than multigravida, where body has been through similar changes before.[23] We found the same as HRV was reduced in primiparous than multiparous participants. Results of Puente ET[24] et al. demonstrated that general autonomic balance is modified by parity effect. Results of study by van der Zwan JE et al. indicated a statistically significant beneficial effect of HRV-biofeedback on psychological well-being for all women, and an additional statistically significant beneficial effect on anxiety complaints for pregnant women.[25] They also suggested the use of HRV-biofeedback as a stress-reducing technique among women reporting stress and related complaints in clinical practice to improve well-being,[25] needed more so for anxious–primigravid women. Indeed, it has long been established that prolonged exposure to stressors incurred at work is linked to a vast array of negative attitudinal, health and, in particular, cardiovascular outcomes for employees.[26]

A healthy heart is not a metronome and entropy of heart rate is a sign of healthy heart. HRV is indicative of health and well being[27] yet under-rated and under-used in countries like India. Pregnancy leads to reduced interplay between higher autonomic nervous system and heart, and the same we saw as reduced power of HRV to one-third. This indicates cardiac compromise even if the pregnancy was normal. Modern era is the era of going beyond conventional subjective instruments like sphygmomanometer more so when one need to screen for discrete cardiovascular parameters like cardiac autonomic status. HRV is a surrogate of cardiac dysautonomia and a validated, objective tool. Providing ante-natal health service is one of the areas of maternal health. Especially pregnancy-induced cardiovascular changes that can lead to aftermaths like hypertensive disorders of pregnancy need a good screening. HRV can be used at a primary care level by family physician to screen those at risk and to monitor progress of the same. This baseline study can be explored further with vertical follow up and with reference to some cardiovascular conditions. There were few limitations to be mentioned here such as small sample, use of 5 min rather than 24 h HRV, complex nature of HRV itself, three subgroups of cases were different not the same individuals, subjective apprehension, lack of baseline HRV data of subjects, and no vertical follow up.

V. LIMITATION

Major limitation of the present study was small sample size. At the same time strength of the study was the longitudinal study design and use of non linear HRV parameters for autonomic function studies in pregnancy.

VI. CONCLUSION

The present study clearly demonstrates that advancing pregnancy is associated with cardiac autonomic imbalance of a large extent, which can be best evaluated by non linear HRV parameters. This finding clearly demonstrates the need for study of non linear HRV parameters, which at present is not being studied in clinical set ups. Further studies with large sample size are needed to clarify and substantiate the complex dynamics of cardiac autonomic imbalance in advancing pregnancy and its clinical significance. At the same time, an urgent need is felt for generation of normative data of both linear and non linear HRV parameters in Indian population as well as for pregnancy, which we aim to undertake in our future research work

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