Spectral Heart Rate Variability During Late Gestation In Moderately Anaemic Pregnancy

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Abstracts: Backround: Third trimester of pregnancy is associated with profound adaptive autonomic cardiovascular changes. Anaemia in pregnancy, which is a common problem in India, is known to put pregnant female at higher cardiovascular risk. The aim of this study is to measure & compare the cardiovascular autonomic balance in normal pregnancy i.e. control group (Hb ≥ 11.0 g/dl) & pregnancy with moderate anaemia i.e. case group (Hb = 7.0 to 9.9 g/dl). Methodology**:** Spectral HRV was measured in supine position using digital polyrite and kubios HRV analysis software. Parameters LF(for sympathetic and parasympathetic modulation) , HF(for vagal modulation) in absolute power (ms ^{2}) and normalised units (n.u.) and LF/HF ratio for sympathovagal balance were measured and analysed using SPSS 16.0 software. Results: A significantly high LF power($p<0.001$) ,low HF power($p<0.001$) and high LF/HF ratio ($p<0.001$) were observed during late gestation period in moderately anaemic pregnant females compared with healthy pregnant females. Conclusion**:** Third trimester of pregnancy with moderate anaemia has an elevated sympathetic activity and reduced parasympathetic activity characterised by compensatory rise in cardiac output mainly because of rise in stroke volume. Spectral HRV is a better test to diagnose above change than mere measuring heart rate and blood pressure. [Kher J NJIRM 2015; 6(2):10-14]

Key Words: HRV (Heart rate variability), LF(Low frequency), HF (High frequency).

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Introduction: Pregnancy itself is associated with profound adaptive changes in maternal hemodynamics. Autonomic nervous system plays a central role in the adaptation of the cardiovascular system to various needs of pregnancy.India contributes to about 80 % of the maternal death due to anaemia in South East Asia.[1] WHO has estimated 65-75 % prevalence of anaemia in pregnant females of India.[2]In India, majority of pregnant women report to antenatal clinic only in 2nd and 3rd trimester. So time available for correction of moderate anaemia is limited, which is generally hypochromic microcytic anaemia.[3]Rang et al [4] argued that since a higher sympathetic nervous activity has been observed in pre-eclampsia, changes in autonomic control preceding the onset of pre-eclampsia could provide early identification ; and this is essential for prophylactic interventions to reduce morbidity and mortality associated with this syndrome.

Different studies have been performed about the etiology of pre-eclampsia but there is not any reliable and cost-effective screening test.[5,6]Although inflammation and extensive endothelial dysfunction of vessels are the main possible mechanisms of pre-eclampsia , but the pathogenesis of this syndrome has not been well understood.[5] Serum biochemical markers have been studied by researchers as potential predictors of pre-eclampsia based on their concentrations during pregnancy [7,8]and their involvement in placental dysfunction. Unfortunately, no single biomarker has been identified as a reliable indicator of predicting pre-eclampsia, rather a combination of biomarkers has been observed to be more dependable .[8] Doppler USG alone is not very reliable predictor and had a high false positive rate of 25% and low detection rate of 63.1%, for pre-eclampsia prediction.[9]spectral HRVprovides information on how the power is distributed (the variance) as a function of frequency, thereby providing a means to quantify autonomic balance at any given time.[10] Lauren M Silva et al [11] have revealed use of HRV with measurement of pulse transit time, a single test, can accurately determine a woman's risk of developing pre- eclampsia.

However, studies on assessment of autonomic functions in anaemic pregnant females are less available. So, In our study we assessed autonomic cardiovascular control in anaemic pregnant females and compared it with normal pregnant females as it can prove valuable, cost-effective, non-invasive screening method for 1) As surrogate model of autonomic dysregulation 2) To predict

and prevent autonomic dysregulation like PIH, Pre - eclampsia, Eclampsia etc.

Material and Methods: After obtaining approval from Institutional Ethical Comittee, spectral HRV was recorded in Applied physiology laboratory from 9.00 a.m. to 11 p.m.at 24^0 C – 26^0 C room temperature ,of pregnant females(25–39 wks of gestation period) attending antenatal clinic of SMIMER hospital, age 18-45 yr, with singleton pregnancy, who were ready to give written informed consent.

In the control group(n = 46), pregnant females with haemoglobin level ≥11.0 g/dl and In a case group(n =52), pregnant females with moderate anaemia having haemoglobin level between 7.0 g/dl to 9.9 g/dl, were assessed.

For both group exclusion criteria were:

- H/o multiple pregnancy (e.g. Twins, triplets, etc.)
- H/o significant illness of any system especially cardiovascular and ventilator system and other illness e.g. malaria ,asthma, tuberculosis)
- H/o habit of smoking ,drugs/alcohol intake or use of therapeutic drugs esp. sympathomimetic drugs/blockers.
- Females with pregnancy induced complication e.g. Hypertension, diabetes, pre-eclampsia, toxaemia of pregnancy.

Subjects were explained the procedure and were asked to avoid tea, coffee, food 2 hrs. prior to study.Anthropometric data (height,weight) were measured on standard measuring scale. Vital data temperature, pulse rate, blood pressure and respiration were assessed in supine position.

For spectral HRVanalysis 5 minute Continuous ECG was recorded from limb leads (lead II) using digital polyrite in supine position and analysed using kubios software version 1.1, from Biomedical signal Analysis Group, Finland.[10]power of LF and HF both in absolute and normalised units as well as LF/HF ratio value of subjects of both group were compared using independant t – test with licensed SPSS 16.0 software. Difference was considered statistically significant between when $p < 0.05$ and highly significant when $p < 0.01$.

Results: No statistically significant difference was observed in age,height,weight and supine pulse rate between both groups (table 1). A significantly high($p = 0.006$) systolic blood pressure (SBP) and significantly low ($p < 0.0001$) diastolic blood pressure (DBP) were observed in pregnant females with moderate anaemia as compared to healthy control group (table 2). A significantly high($p < 0.0001$) LF power ,significantly low ($p < 0.0001$) HF power and significantly high ($p < 0.0001$) LF/HF ratio were observed in pregnant females with moderate anaemia as compared to healthy control group (table 3).

Table – 1: Comparison of mean of anthropometric parameters

parameter	group	N	Mean	SD	p-value
Age (years)	case	52	21.82	2.88	0.427
	control	46	22.32	3.30	
Hb (gm%)	case	52	9.07	0.80	<0.001**
	control	46	11.63	0.73	
Height (cm)	case	52	152.25	7.35	0.870
	control	46	152.02	6.22	
Weight (kg)	case	52	84.60	8.32	0.090
	control	46	81.85	7.48	

*p value is significant and <0.05
** p value is highly significant and <0.01

Table – 2: Comparison of mean of supine pulse rate and BP

parameter	group	N	Mean	SD	p-value
Pulse Rate (bpm)	case	52	91.07	10.67	0.535
	control	46	92.65	14.27	
SBP (mmHg)	case	52	103.94	13.27	0.006*
	control	46	96.10	14.15	
DBP (mmHg)	case	52	91.09	13.89	<0.0001**
	control	46	109.58	12.85	

*p value is significant and <0.05
** p value is highly significant and <0.01

Discussion: No significant difference was observed in supine pulse rate between both group of our study. Lack of oxygenation in tissues due to anaemia results in local accumulation of metabolite like lactic acid due to anaerobic metabolism leading to vasodilatation and consequent increase in HR.[12]

Table – 3: Comparison of mean of spectral HRV parameters

parameter	group	N	Mean	SD	p-value
LF(ms^2)	case	52	110.05	12.22	<0.0001**
	control	46	71.63	10.71	
HF(ms^2)	case	52	72.76	9.19	0.219
	control	46	219.80	858.30	
LF (n.u.)	case	52	45.24	33.91	<0.0001**
	control	46	17.90	13.97	
HF (n.u.)	case	52	15.90	12.65	<0.0001**
	control	46	50.82	31.61	
LF/HF Ratio	case	52	52.20	31.66	<0.0001**
	control	46	28.03	22.15	

*p value is significant and <0.05

** p value is highly significant and <0.01

Data suggested that tachycardia and increased flow velocity are not physiologically adapted to prolonged strain but rather are mechanisms to meet acute bodily stresses such as fever, exercise, hypermetabolism and acute anaemia.[13]Lakhotia et al [14] in their study of clinical assessment of autonomic functions in anaemic noted increase in heart rate ;according to them short circulatory time & peripheral asodilatation occurred as a compensatory mechanism to increase Heart Rate.William B Porter et al [13] has described four mechanisms operating in anaemic patients which may increase the supply of oxygen to tissues when the oxygen carrying capacity of the blood is reduced; under conditions of rest ,a rapid velocity flow and tachycardia with an increase in minute volume of cardiac output (CO) is the first response to anaemia ,as compensation develops tachycardia and increased velocity flow are largely replaced by selective shunting of blood and the removal of an increasing percentage of oxygen in the tissue capillaries from each gram of circulating haemoglobin. A reduction in TPR reduces cardiac work, thus tend to balance the effect of the elevation in CO. In patients with highest CO, tachycardia was not a prominent feature, even breathing 100% oxygen show no change in elevated CO in anaemia.[13,15] Majority of study authors observed no difference in heart rate between healthy pregnant woman and pre-eclamptic woman.[4] During third trimester, a significantly high SBP and significantly low DBP was observed in pregnancy with moderate anaemia as compared to healthy pregnancy in our study. BP is maintained by CO and TPR and these two show significant inverse relationship that is, higher the CO the lower is the vascular resistance. Justus et al concluded it is due to humoral agent, which includes adrenal medullary hormones, V.E.M, serotonin and others.[12] Where as Glick et al [16] postulated a neural mechanism for decrease peripheral vascular resistance.As gestational age increases further, aortocaval compression caused by the enlarging gravid uterus further compromises venous return and CO, leading to a shift in autonomic nervous activity towards an even higher sympathetic and lower vagal modulation in the 3rd trimester of pregnancy.[17]The acute, immediate reversal of the high output state of anaemia by orthostatic stress or by a vasoconstrictor drug indicates that the increased blood flow is primarily mediated by lowered peripheral resistance due to vasodilatation rather than to low blood viscosity.[18,19]Significantly raised power of LF in moderately anaemic group indicates marked increased in sympathetic modulation while a significantly low parasympathetic modulation as evidenced by low HF power and a significantly high LF/HF ratio, a measure of sympathovagal balance, further support it. Although the PIH becomes apparent only in the 3rd trimester of pregnancy, evidence is available that underlying pathophysiological abnormalities appear early in the pregnancy.[20]

R Faber, M Baumart et al [21] had reported that both parasympathetic (HF) and sympathetic (LF) activity is elevated in Hypertensive disorders of pregnancy, indicating an activated autonomic system. The frequency domain analysis of HRV has shown a decrease in the power of HF component in pre-eclamptic pregnancy compared with normal pregnancy: Such a decrease is associated with an increase in LF/HF ratio of HRV.[22] Abdulnasir Hossen et al [23] has revealed that the HF power is reduced in pre-eclamptic pregnancy compared with normal pregnancy at 25-36 weeks of gestation, while LF/HF Ratio increases with pre-eclamptic pregnancy compared with normal pregnancy.While S Rang et al[4] reviewed that compared with healthy pregnant female, pre – eclampsia showed no differences for Heart rate and Blood Pressure

variability, and also no difference in heart rate response to valsalva manoeuvre observed. There is also no difference in BP response to HGT in pre-eclampsia while an inconsistent finding is observed with CPT during pre-eclampsia.[4] Only few studies could demonstrated an increased resting sympathetic activity in pre-eclampsia using direct neurography.[24,25,26]

Conclusion: It is concluded from our study that sympathetic acitivity is raised in form of elevated cardiac output in anaemic pregnancy as compensatory mechanism. Though significantly higher than healthy pregnant female, SBP in anaemic pregnant female was observed in a normal range . So it can't be used as a reliable sole indicator for elevated cardiac output. No significant difference in heart rate indicates that rise in cardiac output is mainly because of elevated stroke volume. Low DBP indicates 1) an additional mechanism to maintain adequate oxygen supply to tissues in anaemia 2) also indicates that venous return is not the primary contributor for elevated cardiac output. So it is concluded that cardiac dimensions and its contractility are mainly responsible for rise in cardiac output. These changes were further supported by raised sympathetic and lowered parasympathetic modulation as measured by spectral HRV. Limitation of this study is finding the sensitivity of spectral HRV to predict cardiovascular complication occurrence which can only be done by extending the study for longitudinal analysis of the same pregnant subjects.

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