Indian Journal of Basic and Applied Medical Research; March 2016: Vol.-5, Issue- 2, P. 611-624

Original article

Evaluation of parasympathetic functions in preeclampsia

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Abstract

Preeclampsia, a common hypertensive disorder, occurs in up to 10% of all pregnancies. It is a disorder of low circulating volume and high vascular resistance. If preeclampsia (toxemia in pregnancy) is considered as an impairment of these hemodynamic alterations, one might expect differences in autonomic control of preeclampsia.Thus,the study was undertaken to assess parasympathetic cardiovascular functions in normalnonpregnant (50),pregnant(50)& preeclamptic pregnant females(50) of 19..29 age group..30/15 ratio, S/L ratio, E/I ratio & valsalva ratio are evaluated and compared among groups. It shows very significant decreased 30/15 ratio & S/L ratio in group II as compared to group I and in group III as compared to Group II.E/I ratio is significantly decreased only in group III as compared to group II. It is concluded that parasympathetic activity is decreased in preclampsia as compared to normal pregnant.

Keywords: Autonomic nervous system, parasympathetic function,preeclampsia

Introduction:

Preeclampsia, the well known complication commonly comes across during pregnancy. Preeclampsia is defined as a pregnancy - specific disorderoccurring after 20 weeks of gestation characterised byblood pressure of 140/90 mmHg or morein pregnancy, on two separate occasionsof at least 0.3 g per 24 hours in a previously normotensive and non-proteinuric patient[1]. It is seen in 10% of allpregnancies and it has a major role in maternalmorbidity and mortality, perinatal death, preterm birthand fetal growth restriction. It occurs in the second halfof pregnancy and resolves shortly after delivery[2]. Despite its prevalence and severity, no comprehensive theory orany phenomenon has been suggested to explain thepathophysiology of this multi system disorder ofpregnancy. Abundant studies described that preeclampsia is characterized by low circulating volume and highvascular resistance, which is exactly opposite of thehemodynamic changes that occur in normal pregnancyi.e. decrease in mean arterial pressure and systemicvascular resistance and marked increase in circulating volume, heart rate and cardiac output. It has been proposed that autonomic nervous system bring about these hemodynamic changes. Cardiovascular adaptations during pregnancy are triggered by decrease in systemic vascular résistance. It results into a feedback response of increase in cardiovascular sympathetic drive to meet the higher circulatory demands of pregnancy. Defect in this feedback response results into preeclampsia.[3]If preeclampsia (toxemia inpregnancy) is considered as an impairment of thesehemodynamic alterations, one might expect differences inautonomic control mechanism of preeclampsia[4]. Methodsfor the assessment of autonomic circulatory control inhumans have therefore been of great interest forresearchers involved in the field of cardiovascularphysiology in pregnancy. The potentialinvolvement of the autonomic nervous systemparticularly parasympathetic nervous system using noninvasive methods like cardiovascular

reflex test inpreeclampsia has, as far as we know, not beeninvestigated much in Indian studies. Since the parasympathetic nervous system also has an importantadaptive influence on the circulation, we decided toevaluate parasympathetic nervous function in preeclampsia, using standard noninvasive cardiovascular reflex test. i.30/15 ratio,S/L ratio,E/I ratio & valsalva ratio.[5,6] These noninvasivemethods have the advantage of minimal risk for themother and the fetus and repeated measurements can bepossible in case of any error in values during procedure.[2]

Aims & objective:

To compare the parasympathetic activity in normal and preeclamptic pregnancy.

Methods:

It is a cross-sectional study, conducted between December 2009 and October 2011 among three groups of subjects.

Group I - Normal non pregnant group (n =50)

Group II – normal pregnant group (n =50).

Group III preeclamptic pregnant (n=50)

Thus a total of 150subjects were included in the study and theselection criterion was:

Preeclamptic pregnant Group (Group III)

Diagnosed cases of Preeclamptic pregnant females (n=50)in the third trimester of pregnancy in the age group of 19to 29years, visiting Obstetrics and gynecology OPD(antenatal clinic) were selected for study. Preeclampsia isdefined as a pregnancy - specific disorder occurring after20 weeks of gestation characterised by blood pressure of140/90 mmHg or higher and proteinuria of at least 0.3 gper 24 hours in a previously normotensive and nonproteinuric patient.[1] All subjects selected wereprimigravida with no other complication of pregnancy.

Exclusion Criteria

Females with

a) Age group other than 19-29

b) Previous history of hypertension, hypotension,CVD, Diabetes mellitus, chronic renal failure,obesity, liver diseases, thyrotoxicosis, vasculardiseases.

c) Multigravida, those < 28 weeks of gestation,multiple pregnancy, known cases of intrauterinegrowth retardation and Eclampsia (In case ofpregnant subjects)

d) Smoking and alcoholics

e) Subjects taking drugs such as hypnotics orautonomic blockers were excluded from thestudy. These exclusion criteria were applied to all groups so as to exclude direct or indirect effects of theabove mentioned factors on the parameters assessed.

Normal normotensive pregnant group (Group II)

For comparison separate group of normal normotensivepregnant females(n=50)of same trimester(thirdtrimester),all primigravida belonging to the same agegroup(19-29years), similar height and weight, and havingsame ethnic group as that of preeclamptic pregnant groupwere enrolled in this group. The selection of this groupwas based on detail history, physical examination as sameas that used for the preeclamptic pregnant group. Theymet same exclusion criteria as that of preeclampticpregnant group.

Normal non pregnant group (Group I)

For comparison separate group of normal nonpregnant females(n=50) belonging to the same age group(19-29yeras), similar height and weight, and having same ethnic group as that of group II & groupIII were enrolled . The selection of this group was based on detail history, physical examination as same as that used for the other groups. They met same exclusion criteria as that of preeclamptic& normal pregnant group.

Procedure

Before starting the study work, all participants were givendetailed information about the project

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and every effortwas taken to solve their queries. This was an attempt toestablish a good rapport with the subjects and relieve theiranxiety. Written informed consent was obtained fromevery subject. The subjects were instructed not to havecoffee, tea cola 12 hours before the tests and were askedto have light breakfast two hours before the tests.[7,8] Thesubjects were asked to report either in the OPD or in the ward of Obstetrics and gynecology as per their convenience in the morning hours for measurement of anthropometric parameters. BP was measured with sphygmomanometer by the standard auscultatory Riva Rocci method and heart rate with the help of ECG machine with lead II, explained in details below. The cardiovascular autonomic tests performed are detailed below in the order of execution. These tests were demonstrated to the subjects.

Anthropometric Measurements

Standing Height - Standing Height of the subject was measured by simply making the subject stand against a wall on which the measuring scale was inscribed. The subject would stand on bare feet on a flat floor against the wall with both the feet parallel and with heels, buttocks and occiput touching the wall. The head was held erect with eyes aligned horizontally and ears vertically without tilt. Then with thehelp of plastic ruler, the top most point of the vertex wasnoted on the wall.[9]

Weight- Weight was measured with KRUPS weighing machine inlight weight garments without foot wears.

Recording of blood pressure

The arterial blood pressure of each subject was recordedin the right brachial artery in sitting position with thepatient's arm at approximate heart level.[10] The subjectswere instructed to come after a night's restful sleep, nostrenuous physical activity to be performed for atleast 1hour before recording the blood pressure. The entireprocedure was explained and the patient madecomfortable to allay rise in blood pressure due to anxiety,excitement or stress.[1,11,12] The blood pressure wasmeasured with sphygmomanometer by the standardauscultatory Riva-Rocci method from the right upperarm. The systolic pressure was recorded as appearance ofthe Korotk off sounds (phase I) and the diastolic bloodpressure recorded as the disappearance of the Korotkoffsounds (phase V)[13].Two readings were taken with a 15minute rest period in between and the arithmetic averageof the two readings was noted as the blood pressure of thesubject.[14,15]

Heart rate

The subject was asked to relax in supine position for 30minutes. The resting heart rate was recorded on astandard ECG from lead II, at a paper speed of 25mm/sec. Two readings were taken with a 15 minute restperiod in between and the arithmetic average of the tworeadings was noted as the heart rate of the subject

HR=1500/R-R interval

Materials

Para sympathetic function tests will be carried out by using

1. Electro cardiograph
2. Sphygmomanometer

Tests for parasympathetic functions

1. 30/15 ratio
2. S/L ratio
3. E/I ratio

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4.valsalva ratio

1) Standing ratio (30/15 ratio):

The 30/15 ratio was calculated using continuous electrocardiogram recording which was recorded when the subject rose to erect posture without any help from supine position. A marker button was used to indicate the point at which the subject started to stand erect .It was calculated by taking ratio of longest R-R interval at beat 30 and shortest R-R interval at beat 15 after standing [10,16].

$$30:15 \text{ ratio} = \frac{\text{Longest R-R interval at 30th beat}}{\text{Shortest R-R interval at 15th beat}}$$

Normal 30:15 ratio is more than 1.04 and when it is less than 1.00 autonomic disturbances are there.[10,16,17].

2) **Standing to lying ratio: (S/L ratio)**

Each subject was asked to stand quietly and then lie down without help while a continuous electrocardiogram was made from 20 beats before to 60 beats after lying down. A marker button was used to indicate the point at which the subject started to lie down. The individual R-R intervals were measured with a ruler from the electrocardiogram and the results expressed as a ratio of the longest R-R interval during the five beats before lying down to the shortest R-R interval during the 10 beats after lying down (standing to lying ratio; S/L ratio). [10,16,18]

$$\text{S/L ratio} = \frac{\text{Longest R-R interval during 5 beats before lying down}}{\text{Shortest R-R interval during 10 beats after lying down}}$$

S/L ratio of >1 was taken as normal &< 1 as abnormal. [16]

3) Deep breathing test:

In the sitting position subject was asked to take deep breaths at the rate of 6 breaths per minute with 5 seconds of inspiration and 5 seconds of expiration for one minute. During this process, continuous ECG monitoring was done with marker to indicate the onset of each inspiration and expiration. The E/I ratio was calculated as: [19]

$$\text{E/I ratio} = \frac{\text{Longest R-R interval during expiration}}{\text{Shortest R-R interval during inspiration}}$$

E/I ratio > 1.20 is taken as normal. [20]

4) Valsalva ratio:

The heart rate response in the Valsalva maneuver is measured using the Valsalva ratio(VR).[21]

The subject was seated comfortably and was asked to blow into mouth piece connected to a mercury sphygmomanometer and holding it at a pressure of 40 mmHg of mercury for 15 seconds, while a continuous ECG was being recorded. The ECG was continued to be recorded after release of pressure for 30 seconds. Valsalva ratio was calculated as the ratio of maximum R-R interval after the maneuver to minimum R-R interval during the maneuver ([10,16].

$$\text{VR} = \frac{\text{Longest R-R interval after the strain}}{\text{Shortest R-R interval during the strain}}$$

A ratio greater than 1.45 is normal, 1.20-1.45 is borderline and less than 1.20 is abnormal . [10,16]

Statistical analysis: [22,23].

Statistical analysis of the observations was carried out using SSPS version 17.0 and graph pad version 5.0. The data was expressed in terms of mean and standard deviation and inferential statistics was determined using the one way analysis of variance (ANOVA), Bonferroni's multiple comparison test and z test as appropriate.

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Statistical significance was tested at 5% and expressed in terms of 'p' value with $p<0.05$ = statistically significant.

Results

Following anthropometric parameters were assessed and autonomic function tests were carried out in each of the study groups.

Anthropometric parameters

1. Standing height
2. Weight
3. Body mass index (BMI)
4. Arterial blood pressure

Table1. Table showing the distribution of cases in the study group

Group I Non-pregnant women		Group II Normal pregnant women		Group III Preeclamptic women	
5	0	5	0	5	0

Table 2. Table showing groupwise comparison of age of subjects.

	Group I Nonpregnant Wome	Group II Normal pregnant W	Group III Preeclamptic Women	Group I vs Group II	Group II vs Group III
Age (years)	22.26 ± 2.67	23.08 ± 2.76	23.58 ± 2.90	p > 0.05 NS	p > 0.05 NS

The above tables shows the age (in years) of the three groups of subjects expressed in terms of mean and standard deviation. There was no statistical difference in the mean age of normal non pregnant (Group I),normal pregnant(Group II) & preeclamptic pregnant females (Group III).

Table 3. Table showing group wise comparison of height, weight and BMI of subjects

	Group I Nonpregnant Wor	Group II Normal pregnant Wom	Group III Preeclamptic Wom	Group I vs Group II	Group II vs Group III
Height (metres)	1.56 ± 0.05	1.55 ± 0.04	1.54± 0.03	p > 0.05 NS	p > 0.05 NS
Weight (Kg)	50.7± 2.92	59.68 ± 4.94	60.52 ± 2.59	p < 0.001 ***	p > 0.05 NS
BMI (Kg/m^2)	20.66 ± 1.589	24.69 ± 2.342	25.41± 1.604	p < 0.001 ***	p > 0.05 NS

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The above table shows the mean height, weight and BMI of the three groups of subjects with their standard deviation. There was no statistical difference (p>0.05) in the heights of Group I, Group II and Group III.

The weight of Group II was significantly (p <0.001) increased as compared to Group I, whereas no statistically significant difference in the weights of Group II & Group III.(p>0.05).

Similarly there was significant increase (p<0.001) in the BMI of Group II as compared to Group I but not so in case Group III when compared to Group II.

Table 4. Table showing the gestational age of the pregnant subjects i.e. Group II and Group III.

	Group II Normal pregnant Women	**Group III Preeclamptic Women**	**Group II vs Group III**
Gestational age (weeks)	31.62 ± 2.303	31.92 ± 1.861	p > 0.05 NS

The above table shows the comparison of the gestational age of Group II and Group III. There was no significant difference between the two groups with respect to gestational age.(p >0.05).

Table 5.Table showing group wise comparison of the blood pressure of subjects.

	Group I Nonpregnant Wome	**Group II Normal pregnant Wo**	**Group III Preeclamptic Women**	**Group I vs Group II**	**Group II vs Group III**
Systolic blood pressure (mm Hg)	116.6 ± 7.808	113.9 ± 7.655	154.8 ±4.675	p > 0.05 NS	p < 0.001 ***
Diastolic blood pressure (mm Hg)	75.88 ± 5.472	70.72 ± 6.058	100.4 ± 9.510	p < 0.001 ***	p < 0.001 ***
Mean arterial pressure (mm Hg)	89.47 ± 4.710	85.12± 4.392	118.5 ± 6.401	P < 0.001 ***	P < 0.001 ***

This table gives the systolic, diastolic blood pressure and the mean arterial pressure expressed in terms of mean and standard deviation of the three groups of subjects.

There was no significant difference in the systolic blood pressure (SBP) between Group I and group II (p>0.05).

The Group III showed significant increase in the systolic blood pressure as compared to Group II (p < 0.001).

The diastolic blood pressure (DBP) of the Group II was significantly lower than that of the Group I (p < 0.001) whereas the Group III had a significantly higher diastolic blood pressure as compared to the Group II (p < 0.001).

Similarly the mean arterial pressure (MAP) of the Group II was significantly lower than that of group I (p <0.001). The Group III had a significantly higher mean arterial pressure as compared to Group II (p < 0.001)

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Table 6. Table showing groupwise comparison of Resting Heart rate of subjects.

	Group I Nonpregnant Wome	Group II Normal pregnant W	Group III Preeclamptic Wome	Group I vs Group II	Group II vs Group III
Resting Heart rate (HR)	76.32 ±10.16	87.3 ±14.01	91.1± 5.79	P<0.001 ***	P>0.05 NS

This table gives the resting HR expressed in terms of mean and standard deviation of the three groups of subjects.

There was significant increase in HR in Group II as compared to Group I ($p< 0.001$).Group III showed increase in HR as compared to group II but it was found to be non significant ($p>0.05$).

Table 7. Table showing groupwise comparison of the parasympathetic function of the subjects in all three groups.

Response to Parasympathe-tic function tests	Group I Nonpregnant Wome	Group II Normal pregnant W	Group III Preeclamptic Wome	Group I vs Group II	Group II vs Group III
30/15 ratio	1.313±0.195	1.206 ±0.157	1.110±0.133	p<0.01 **	p<0.01**
S/L ratio	1.047± 0.088	0.948 ± 0.184	0.862 ±0.154	p<0.01**	p<0.01**
E/I ratio	1.300±0.114	1.263±0.114	1.211±0.111	p>0.05 NS	p<0.05 *
Valsalva ratio	1.599 ±0.169	1.533±0.1969	1.479± 0.1180	p > 0.05 NS	p > 0.05 NS

This table gives 30/15 ratio. Standing to lying ratio(S/L ratio), deep breathing ratio (E/I ratio) and valsalva ratio (VR) expressed in terms of mean and standard deviation of the three groups of subjects.

30/15 ratio is significantly decreased in group II & group III as compared to group I & group II respectively. Similarly significant decreased S/L ratio was found in group II and group III as compared to group I & group II respectively. There was no significant difference in E/I ratio in group I & group II whereas significant decrease in E/I ratio was found in group III as compared to group II. No significant changes were found in VR in group II and group III when compared to group I & group II respectively.

Discussion:

In the present study, no significant difference in age,height, weight or BMI was found amongst the groupsstudied indicating that the groups were comparable.

Blood pressure

There is a significant increase in the systolic blood pressure, diastolic blood pressure and mean arterial

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blood pressure of the preeclamptic group as compared to normal pregnant.

Resting Heart rate

The preeclamptic pregnant group shows increase in mean resting heart rate as compared to the normal pregnant group, but it is non significant.

Standing ratio (30/15 ratio):

The mean30/15 ratio of the group I and group II were 1.313 and 1.206 respectively. Thus there is an significant decrease in mean 30/15 ratio ($p< 0.01$) of group II as compared to Group I (Group I vs group II).The finding of the present study is in conformity with findings of earlier studies Bachlaus N et al(2010) [24], Eva ekhlom et al 1994 [25] ,Rang SA et al(2002) [2].

Standing up causes a fall in blood pressure and a reflex tachycardia (heart rate increase i.e shortening of RR interval) at 15th beat. The subsequent decrease in heart rate (bradycardia i.e lengthening of RR interval) is associated with recovery of the arterial blood pressure and is mediated via the arterial baroreflex with vagal efferent fibres.[2] In this study, decrease in 30/15 ratio in pregnancy implies that the induced bradycardia is diminished during pregnancy, which is explained by the decrease in baroreflex activity. In addition to altered parasympathetic activity**,** increased blood volume during pregnancy may also contribute to this phenomenon [26] .**Brooks VL et al** explained insulin resistance as one of the mechanism in decreasing baroreflex sensitivity in pregnancy. [27]**Daubert DL et al** suggestedthe mechanism how insulin resistance appears in pregnancy & how it affects the baroreflex function. Pregnancy-induced insulin resistance develops secondary to the actions of several hormones, including glucocorticoids, estrogen, progesterone, placental lactogen, and TNF. These hormones may decrease insulin sensitivity by increasing free fatty acid levels, which can inhibit insulin signaling by serine phosphorylation of the insulin receptor and insulin receptor substrate proteins [28].

The brain is the site at which pregnancy depresses baroreflex function[29]. Insulin receptors are present in numerous but discrete sites in the brain, many of which interact with brain stem baroreflex pathways. Moreover, insulin gains access from the systemic circulation to the brain via trans endothelial transport across the blood-brain barrier[30,31], and in insulin resistant states, insulin transport is reduced, resulting in decreased brain insulin concentrations. Because insulin acts in the brain to enhance baroreflex gain, decreased brain insulin concentrations may underlie the impaired baroreflex gain[28]. **Hines T et al**showednitric oxide (NO) is responsible for decreasing baroreflex sensitivity. NO is known to suppress baroreceptor activity and pregnancy associated with increased synthesis of NO[32].

Group III (mean ratio of 1.11) has significant decrease in standing ratio ($p< 0.01$) as compared to group II (mean ratio of 1.206).(Group II vs group III).The finding of the present study is in conformity with findings of- K E J Airaksinen et al[4],E Ekhlom et al (1994) [33],EJM Wouters et al[7]. This decrease in ratio implies that induced bradycardia is significantly diminished in preeclamptic group as compared to normal pregnant group i.e.decrease baroreflex induced slowing of heart rate in pregnancy(as discussed above) & further decrease in baroreflex induced slowing of heart rate in preeclampsia . Autonomic hemodynamic disturbances, reflected in decrease ratio in preeclampsia, is explained by further decrease in baroreflex sensitivity, cited in a study by **Ekholm EMK et al study**[33] Decrease in 30/15 ratio in pregnancy suggest decrease in the vagal reactivation which further decreases in preeclampsia. Decrease in vagal tone in preeclampsia quoted by **Pal GK et al** [34]**.**

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Decrease in baroreflex activity is explained by decreased baroreflex sensitivity in pregnancy, which is further decreased in preeclampsia. This is in conformity with earlier studies: **Silver HM et al(2001)**[35] & **R Faber et al(2004)**[36] demonstrated that baroreflex gain and sensitivity is significantly reduced in pregnancy in comparison to non pregnant state and it is is further reduced in preeclamptic pregnancy.

Insulin resistance, one of the important causative factor in decreasing sensitivity[27] and how it is related to pregnancy & preeclampsia is explained below:Pregnancy is characterized by insulin resistance[37], as discussed above and it is one of the cause behind decreased baroreflex sensitivity. Preeclampsia is characterized by greater degree of insulin resistance than normal pregnancy[38,37]. Thus, it is possible to have greater degree of decreased baroreflex sensitivity in preeclampsia when compared to normal pregnancy.**Molino et al** [39] observed decreased baroreflex control of heart rate in preeclampsia . It might be the reason behind decrease ratio in preeclamptic pregnant as compared to normal pregnancy.

Dorette A et al [40] suggested low plasma volume in preeclamptic women is associated with decreased baroreflex sensitivity. **Airaksinen KEJ et al** [4] cited in their study that autonomic nervous system dysfunction in preeclampsia may result from direct injury to nerve fibres or latent central nervous system involvement.**Kaaja RJ et al**[41] studied the postural effect in preeclamptic, normal pregnant and non pregnant women. He observed that plasma nor epinephrine levels were higher in preeclampsia than normotensive pregnant women and was most obvious in upright position. Preeclampsia is associated with sympathetic over activity as reflected by plasma nor epinephrine levels, mostly in upright position. Furthermore parasympathetic withdrawal might contribute to the hemodynamic abnormality in preeclampsia[41].

Standing to lying ratio:

The mean standing to lying ratio of the group I and group II were 1.047 and 0.948 respectively. Thus there is a significant decrease in mean standing to lying ratio ($p<0.01$) in normal pregnant women as compared to non pregnant (Group I vs Group II).

Normally, Heart rate response to lying down shows reflexly, a brief initial rise due to Bainbridge reflex. Venous engorgement of right atrium shows reflex increase in heart rate .While in case of pregnancy in lying down position, aortocaval compression decreases venous return to atrium[42] resulting in less stimulation of reflex. Thus, it showed less increase in heart rate response to lying down position. It is reflected in decrease S/L ratio in pregnancy, which implies that vagal impairment is present in pregnancy. Other possible mechanisms that involved are already discussed above in standing ratio i.e baroreflex induced bradycardia is seen while standing for 30sec or more and it is decreased in pregnancy which contribute to decrease in standing to lying ratio also.

Chen GY et al [43,44]studied heart rate response to supine and standing posture using heart rate variability (HRV) analysis and found reduction in vagal activity in pregnancy in supine position.

The preeclamptic group (mean=0.862) has significant decrease ($p<0.01$) in standing to lying ratio as compared to the normal pregnant group (mean =0.948)(Group II vs Group III).

When compared to normal pregnancy, aortacaval compression is present in both the groups but along with that decrease blood volume in preeclamptic group contributes to further decrease in venous return [40] .It results into further decrease in stimulation of reflex, resulted into decrease in the rise in heart rate. It is reflected in

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decrease S/L ratio in preeclampsia as compared to pregnancy implying further impairment of vagal activity in preeclampsia.

Deep breathing:

The mean E/I ratio of the non-pregnant (group I) and normal pregnant groups (group II) were 1.3 and 1.263 respectively. Thus, there is non significant decrease in mean E/I ratio ($p>0.05$) of group II as compared to group I.(Group I vs group II)

The finding of the present study is in accordance with findings of earlier studies of Eeva Ekhlom et al (1996) [45], Rang SA et al(2002).[2]

Respiratory fluctuations in heart rate i.e. inspiration induced tachycardia (shortest RR interval) and expiration induced bradycardia (longest RR interval) , reflected in E/I is mediated by baroreflex mechanism with vagal fibres as efferent pathway[2,16,20]. Heart rate response is found to be significantly decreased in pregnant women as compared to normal nonpregnant women. Decrease in heart rate response could be explained as mechanical impairment of the ability to breath deeply due to growing uterus in pregnant women. It is found that non significant decrease in E/I ratio ,suggesting decrease in parasympathetic activity in pregnancy. As baroreflex mechanism is also involved in modulating heart rate during deep breathing, so any impairment in baroreflex function results in parasympathetic dysfunction.

Mechanism that alter baroreflex activity includes insulin resistance, mechanical factors related to stretch or distortion of the nerve endings as well as humoral factor such as endothelial derived growth factors and circulating hormones.[32]

One of the mechanisms of decreased baroreflex activity has been suggested that it might be due to alterations in the cardiac discharge pattern or cardiac receptor subtypes.[45]

Pregnant rats are found to be hyponatremic [32] and this is also true in case of human beings. **Thoren et al** observed that hyponatremia could play a role in attenuated baroreceptor discharge.[32]

The mean E/I ratio of the normal pregnant (Group II) and preeclamptic pregnant group(group III) were 1.263 and 1.211 respectively. Thus, the group III has significant decrease in E/I ratio ($p<0.05$) as compared to group II. (Group II vs Group III)

The finding of the present study is in accordance with findings of earliest studies - K E J airaksinen (1985) [4], Eeva M K Ekholm (1994) [21].

It is found that mean E/I ratio is significantly decreased in preeclampsia when compared to normal pregnancy. Decrease in E/I ratio (i.e. decrease heart rate response to deep breathing reflect an excessive decrease of parasympathetic control of heart ratesuggesting decrease in vagal control of heart rate.

Non invasive study by **Enroth et al**[47] using heart rate variability, suggested that vagal control of heart decreased during preeclampsia.**Sower et al** demonstrated that hyperinsulinemia and insulin resistance are associated with preeclampsia in African-Americans.[48]

The depressed baroreflex function observed during normal pregnancy appears to worsen in pregnancy associated diseases such as preeclampsia .This is in conformity with earlier studies [35,39,49].This could be one of the reason for decreased heart rate response in preeclampsia compared to normal pregnancy.

Seligman et al&Wasserstrum Net al suggested decrease in baroreflex sensitivity in preeclampsia as compared to pregnancy.[50,51] **Brooks VL et al** observed that decreased baroreflex sensitivity is due to insulin resistance which is also a characteristic feature of pregnancy.

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Preeclampsia is associated with greater degrees of insulin resistance than that of pregnancy which could explain more decreased baroreflex sensitivity in preeclampsia as compared to normal pregnancy.[27] **Ekholmet al** suggested thatthe maladaptation of the cardiovascular system in women with pregnancy-induced hypertension is manifested as a lack of the physiologic decline in cardiovascular oscillations.[52]

Valsalva ratio:

The mean valsalva ratio of the non-pregnant (Group I) and normal pregnant group(Group II) were 1.599 and 1.533 respectively **.**There is decrease in the mean valsalva ratio in group II as compared to Group I, but it's found to be non significant. ($p > 0.05$, NS).(Group I vs Group II)

The finding of the present study is in accordance with the findings of earlier studies- Rang SA et al (2002) [2] , Hans schobel et al(1996) [6] , Eeva ekholm (1996) [45],Eeva M K kholm (1994) [25], Souma ML cannabis CD(1983).[53]

During the Valsalva maneuver, the increased intrathoracic pressure reduces the return of venous blood to the heart. This leads to a reduction of the blood pressure and a baroreceptor mediated tachycardia. When the strain is released, blood pressure rises and a reflex bradycardia ensues. The bradycardia is due to vagalactivity but the cause of the tachycardia is controversial.[2,10,16]A diminished Valsalva ratio during the second and third trimesters of pregnancy probably results from a reduced functioning of baroreceptors, an integral part of baroreflex pathway.

Ekholm et al[25] explained that the physiological reduction of venous return during the strain is balanced off and less marked because of the increased blood volume in pregnancy. This may result in smaller blood pressure changes during and after the strain and, consequently, in reduced changes in the heart rate. Thus, decreased baroreflex mediated changes can be attributed to decreased baroreflex in the pregnancy. Similar result were found in study of Souma ML et al. [53]

Normal pregnant group (Group II) & preeclamptic group (Group III) showed mean valsalva ratio of 1.533 & 1.479 respectively. There is decrease in ratio in group III as compared to group II, but it is found to be non significant.(Group II vs Group III)This is in accordance with the findings of earlier studies Hans schobel et al [6] ,Rang SA et al [2],Eeva M K ekholm 1994 [21] .

Reduced valsalva ratio in the valsalva maneuver reflect excessive decrease of parasympathetic cardiac control i.e. decrease vagal control of heart rate. Thus, decrease in valsalva ratio suggest decrease vagal control of heart rate in preeclampsia. Decreased vagal tone was found in study of heart rate variability in preeclampsia.[47]As discussed above, vagal control of heart is modified by baroreflex ,so this decrease in parasympathetic cardiac control i. e. decrease in vagal activity can be attributed to decrease in baroreflex function and this baroreflex function is further decreased in preeclampsia when compared to normal pregnancy. [35,39,49,51]

Mechanism for alterations in baroreflex function during pregnancy are not known; however little is known, about possible gestational changes in the baroreceptor itself. Attenuated afferent discharge in response to a pressure stimulus could also contribute to blunted reflex effects. However mechanism that alter baroreflex activity includes insulin resistance, mechanical factors related to stretch or distortion of the nerve endings as well as humoral factor such as endothelial derived growth factors and circulating hormones. [32].Insulin resistance is seen in pregnancy & is more prominently more seen in

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preeclampsia. How insulin resistance decreases baroreflex sensitivity is explained above.

Conclusion:

As preeclampsia is found to be autonomic dysfunction disorder, then recent technique like pranayam and yoga could be beneficial in prevention of progress of disease as yoga practices bring about stable ANS equilibrium with tendency towards parasympathetic nervous system dominance and also cardiovascular efficiency is increased as many cardiovascular diseases are associated with it. Next to the application of preventive strategies, early prediction using the same autonomicfunctions could also be useful for targetingobstetrics care at those most likely to benefit

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