National Journal of Medical and Allied Sciences

[ISSN Online: 2319 – 6335, Print: 2393 – 9192|Original article |Open Access]

Website:-www.njmsonline.org

PREECLAMPTIC PREGNANCY EMPLOYING TIME DOMAIN ANALYSIS IN HEART RATE VARIABILITY STUDY

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Abstract

Background: Preeclampsia is a disorder characterized by development of hypertension to the extent of 140/90 mm Hg or more with proteinuria after 20th week of pregnancy in a previously normotensive and non proteinuric woman. Physiologically blood pressure is controlled by autonomic nervous system (ANS) so study of ANS during pregnancy plays a significant role to extract some vital information which may be helpful to deal with pregnancy induced hypertension (PIH) or Preeclampsia. The main objective of our study was to compare the maternal time domain indices of Heart rate variability (HRV) changes between normal pregnancy and preeclamptic pregnancy.

Methods: Fourty eight subjects (33 of normotensive pregnant women i.e, control group and 15 preeclamptic pregnant women i.e, study group) of more than 20 weeks pregnancy were recruited from the obstetrics & gynaecology department of JNMC, AMU, Aligarh. Physical examination was done and anthropometric measurement like height & weight were taken. Urine test was conducted to every pregnant woman for urine albumin and we designated the pregnant women as preeclamptic women on the basis of definition. The collected data was statistically analysed using HRV analysis software.

Results: No significant difference in body mass index was observed between the two groups. Systolic blood pressure and Mean arterial pressure of study group was significantly higher than control group. Values of all the components of time domain analysis of HRV were significantly decreased among the preeclamptic women than normotensive pregnant women.

Conclusion: The present study indicates that the contribution of anthropometric parameters to the blood pressure changes in pregnancy is negligible. Significant decrease in all the three components of time domain indices was observed in preeclamptic pregnant women than normotensive pregnant women which indicates that parasympathetic tone was decreased in preeclampsia. Vagal withdrawal and sympathetic exaggeration may be the possible cause of preeclampsia in pregnant women.

Keywords: Preeclampsia, heart rate variability, pregnancy, autonomic nervous system

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Introduction:

Preeclampsia is the most serious medical disorder of pregnancy and constitutes a major cause of maternal and perinatal morbidity and mortality [1, 2]. It is characterized by development of hypertension to the extent of 140/90 mm Hg or more with proteinuria after 20th weeks of pregnancy in a previously normotensive and non proteinuric woman [3]. In India, pregnancy-induced hypertension (PIH) accounts for about 50,000 deaths per year [4]. Physiologically blood pressure is controlled by autonomic nervous system (ANS) so study of ANS during pregnancy plays a significant role to extract some vital information which may be

helpful to deal with PIH or Preeclampsia [5].The autonomic nervous system and its changes during different pathophysiological conditions could be evaluated with heart rate variability analysis test. The pathophysiology of development of hypertension is due to decrease in size or increase in volume of vascular compartment but in PIH, hypertension develops due to low blood volume which signifies the role of sympathetic over activity in causing severe vasoconstriction [6]. Time domain analysis of heart rate variability's (HRV) is a sophisticated, noninvasive tool for the detection of ANS regulation of the heart. In the field of Obstetrics & Gynecology, HRV is especially suitable for pregnant women because it is virtually noninvasive and produces the least stress on the mother and the infant. High HRV is a sign of good adaptation indicating the efficient functioning of ANS. Conversely, low HRV signifies inadequate adaptation of the ANS, indicating physiological malfunction. This HRV analysis can be performed by frequency domain and time domain measures. Time domain measures are the means and standard deviations of R-R intervals obtained by continuous ECG, where NN (normal –to- normal) indicates all R-R intervals. The simplest variable to calculate is the standard deviation of the NN interval (SDNN) .Since variance is mathematically equal to total power of spectral analysis, SDNN reflects all the cyclic components responsible for variability in the period of recording. The most commonly used measures derived from interval differences include RMSSD, the square root of the mean squared differences of successive NN interval [7]. The modification in the autonomic control occurs during pregnancy and its evaluation through Heart rate variability (HRV) analysis is a very informative technique now a day. This study was conducted to compare the maternal time domain HRV changes between normal pregnancy and preeclamptic pregnancy.

Material and methods:

The present study was conducted in autonomic lab of department of physiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh between the periods of June 2014 to August 2014. After obtaining the approval of the project from institutional ethical committee 48 subjects (33 normotensive pregnant women i.e., control group and 15 preeclamptic pregnant women i.e., study group) of more than 20 weeks pregnancy were recruited from the outpatients department, antenatal unit and wards of obstetrics and gynecology department. Written informed consent was obtained from all the females prior to initiation of the study. All the subjects were explained about the procedure to be undertaken. Subjects of study group included pregnant women who had risk factors for PIH so inclusion criteria for the study group included established risk factors for PIH such as family history of preeclampsia, preeclampsia in previous pregnancy, extremes of reproductive age, BMI >35, diastolic blood pressure >80 mm Hg at the first visit, underlying medical conditions (diabetes mellitus, renal disease, preexisting hypertension). Subjects of control group included pregnant women who had none of above mentioned risk factors for preeclapmsia. All the subjects were examined and detailed personal history was taken with reference to smoking, alcohol intake, family history of hypertension, socioeconomic status, place of residence etc. All subjects had to fill a performa. Physical examination was done and anthropometric measurements like height and weight were taken. BMI was calculated as per quetlet's index. Urine test for albumin estimation was done. Pregnant women were defined as preeclamptic, if there was presence of total protein in 24 hours urine of more than >1+ (0.3 gm/L) or ≥ 2+ (1 gm/L) on at least two random clean catch urine sample tasted ≥4 hours apart in the absent of urinary tract infection [3]. The subject was advised to take complete bed rest in supine position for 15 minutes in a cool and calm environment and not to take and perform physical or mental activity. Blood pressure was recorded using mercury sphygmomanometer. The recording of short term HRV was done according to recommendation of the task force. Following 10 minutes of supine rest in autonomic laboratory of our department of physiology, all leads of HRV were placed over the subject in requisite position. Lead II of ECG was recorded during supine rest using Medicaid 4 channel system. The data was

transferred from Medicaid machine to window based computer with HRV analysis software. Best possible artifact and ectopics were removed. Time domain indices such as mean RR, standard deviation of normal to normal intervals (SDNN) and square root of the mean square differences of successive normal to normal intervals (RMSSD) of HRV were calculated. We used unpaired t-test for statistical analysis and observe the change between the two groups.

Results:

Table 1 shows the comparison of the anthropometric parameters between normotensive and preeclamptic pregnant women. No significant difference was present between the two groups. Table 2 shows that the systolic blood pressure and mean arterial pressure of study group was significantly higher than control group while diastolic pressure was not significantly higher. Table 3 shows that Mean R-R, SDNN and RMSSD of preeclamptic women were significantly decreased than the normotensive pregnant women.

Table 1: Anthropometric parameters between normotensive and preeclamptic pregnant women

Anthropometric measurement	Normotensive pregnant women (control group)	Preeclamptic pregnant women (study group)	Normotensive versus preeclamptic
	Mean ± S.D	Mean± S.D	p-value
Age (yrs)	26.27 ± 2.10	26.80 ± 5.81	0.7885
Height (mts)	155.73 ± 5.10	151.20 ± 4.38	0.1092
Weight (kgs)	58.95 ± 10.79	57.00 ± 8.216	0.1092
BMI	24.26 ± 3.94	26.26 ± 3.46	0.3876

Table 2: Blood pressure parameters among normotensive and preeclamptic pregnant women

Blood Pressure (mm Hg)	Normotensive pregnant women (control group)	Preeclamptic pregnant women (study group)	Normotensive versus Preeclamptic
	Mean ± S.D	Mean ± S.D	p-value
Systolic BP	116.55 ± 15.08	137.20 ± 5.40	0.0109*
Diastolic BP	79.45 ± 9.55	83.60 ± 13.74	0.4929
Mean Arterial Pressure	91.81 ± 10.88	105.20 ± 5.576	**0.0228***

Table 3: Time domain parameters between normotensive and preeclamptic women

Time domain analysis	Normotensive pregnant women (control group)	Preeclamptic pregnant women (study group)	Normotensive versus Preeclamptic
	Mean ± S.D	Mean ± S.D	p- value
Mean R-R (secs)	0.628 ± 0.0573	0.542 ± 0.071	**0.0210***
SDNN (secs)	0.0166 ± 0.007	0.0072 ± 0.003	**0.0161***
RMSSD (ms)	9.827 ± 4.862	5.00 ± 0.869	**0.0482***

*** p<0.05 statistically significant**

Discussion:

In the present study the anthropometric parameters (age, height, weight and body mass index) of normotensive pregnant women (control group) were matched with preeclamptic pregnant women (study group) and the two group have no significant changes. In the pregnancy increased BMI is mainly due to increasing size of growing fetus, uterus, placenta and increase in ECF volume but not because of increased adiposity [8] so in our study overall contribution of anthropometric parameters to the blood pressure changes in pregnancy is negligible as the co-relation between the two groups was not significant. The blood pressure measurement in our study observed that preeclamptic pregnant women (study group) have higher systolic and mean arterial blood pressure than normotensive pregnant women which could be due to increased sympathetic tone as few studies defined preeclamptic pregnancy is a state of sympathetic overactivity [9,10]. The diastolic blood pressure which is an index of peripheral vascular resistance was also higher in study group but not differ significant with control group. It also reflect the basal sympathetic tone [11] so sympathetic activation may be the cause of elevated blood pressure in preeclampsia in our study. This observation was supported by the study of Schobel et al (1996) [9] and Visser et al (1991) [10]. Time domain analysis of heart rate variability in our study showed that there were three components recorded in time domain analysis i.e, Mean R-R, Standard deviation of normal to normal intervals (SDNN) and Square root of the mean squared differences of successive normal to normal intervals (RMSSD).

These three indices are mainly the indicators of parasympathetic activity. In the present study significant decrease in all the three component of time domain indices was observed in preeclampsic pregnant women than normotensive pregnant women. It indicates that parasympathetic tone was decreased in preeclampsia. SDNN and RMSSD reflect vagal modulation of heart rate. It means that mild decrease in parasympathetic modulation occur on SA node discharge. These all calculated indices reflect vagal modulation of heart rate and its contribution was more than sympathetic activation [12]. Same results were obtained by the study of Yang et al (2000) [13], Shyma et al (2008)[14], Pal et al (2011)[12] and Hossen (2013)[15]. The changes occurs in preeclampsia is not fully understood but few studies observed that some biologically active factors like cytokines or reactive oxygen species from placenta which inhibit vascular relaxation pathway or facilitates vascular smooth muscle contraction, may be responsible for hypertension in pregnancy[16]. Medullary cardiovascular centre in the brain which modulate central parasympathetic outflow may be affected by these placental factors. Reports from various studies indicates that these placental factors cytokines [17,18]. and reactive oxygen species[18,19] released peripherally cross blood-brain barrier and influence activities of various brain centers and their estimation may be helpful for the further research. Our study on time domain analysis suggested that vagal withdrawal and sympathetic exaggeration may be the possible cause of preeclampsia in pregnant women.

Conclusion:

The present study conducted with the objective to compare the maternal HRV changes (Time domain analysis) between normal pregnant women & preeclamptic pregnant women it clearly indicates that the contribution of anthropometric parameters to the blood pressure changes in pregnancy is negligible between the two group and sympathetic activation may be the cause of elevated blood pressure in preeclamptic pregnant women of Aligarh district. The time domain analysis of heart rate variability proved as a good tool in the study of preeclampsia. Significant decrease in all the three component of time domain indices was observed in preeclampsic pregnant women than normotensive pregnant women which indicates that parasympathetic tone was decreased in preeclampsia. SDNN and RMSSD reflect vagal modulation of heart rate. It means that mild decrease in parasympathetic modulation occur on SA node discharge. Our study on time domain analysis suggested that vagal withdrawal and sympathetic exaggeration may be the possible cause of preeclampsia in pregnant women. Our study could have been better if this study will be conducted in large sample size or it would be conducted in different trimester of pregnancy. If our study would have been started between non pregnant and pregnant women, we could be able to know how much HRV changes have been taken place during these two phases i.e, pregnant and non pregnant state. Then we could further extend our study for HRV changes between pregnant and preeclamptic women where both groups are in pregnant state. Further these findings could help in observing the HRV changes among three different phases i.e, non pregnant, pregnant and preeclamptic phase. Further this study could be better if we estimate the levels of placental factors (cytokines and reactive oxygen species) in both the groups along with the level of proteinuria.

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Conflicts of Interest: None Funding: None

Citation: ***Khan GAN, Ishrat N. Preeclamptic Pregnancy Employing Time Domain Analysis In Heart Rate Variability Study. National Journal of Medical and Allied Sciences 2014; 3(2):15-19***