

Variations in Auditory Reaction time with Systolic and Diastolic Blood Pressure in Pregnancy Induced Hypertensive females compared to Healthy Normotensive Pregnant females in third trimester

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Abstract

Objective: Auditory reaction time (ART) is time required for purposeful voluntary response to auditory stimuli. It includes the time required in central information conducting process hence can diagnose quantitative auditory function of the central auditory pathway and also the cognitive ability of subjects. Pregnancy Induced Hypertension (PIH) was studied to cause impairments in auditory functions of the female during third trimester due to raised blood pressure. PIH is profound disorder prevalent in 2-3% population worldwide causing high mortality and morbidity. PIH also has been found to cause cognitive disabilities later in life. Present study was conducted to evaluate the responsiveness and cognitive disabilities developed because of raised blood pressure. **Methods:** Cases were 50 Pregnancy Induced Hypertensive and Controls were age matched 50 Normotensive Pregnant Females both in third trimester. ART was measured by computer based reaction time software in all the cases and controls. During the reaction time testing, auditory stimuli was given for three times and minimum reaction time was taken as the final reaction time for that sensory modality of that subject. The results were statistically analyzed and were recorded as Mean \pm S.D and Student's paired *t*-test was applied to check the level of significance. **Results:** Study showed that ART in Pregnancy induced Hypertensive females was significantly raised when compare to Healthy Normotensive Pregnant females. Values of ART was found significantly increased in multiparous pregnancy induced hypertensive females when compare to primiparous pregnancy induced hypertensive females. **Conclusion:** Pregnancy induced Hypertension can be concluded to cause damage to all the body tissues including the central and peripheral nervous system. Mental processes are involved in identification of stimulus, response selection, and programming and this takes certain time which was more in females with PIH when compared to healthy normotensive Pregnant females. Widespread endothelial damage and dysfunction, systemic toxicity, coagulation defects, and an increased systemic inflammatory response, poses risk factors for hearing disorders during PIH.

Key words: ART, PIH, Blood Pressure, Cognitive disabilities.

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Introduction

Auditory reaction time (ART) is time required for purposeful voluntary response to auditory stimuli. It includes the time required in central information conducting process hence can estimate quantitative auditory function of the central auditory pathway and also the cognitive ability of subjects.

Simple auditory reaction time is the time interval between the onset of the single stimulus and the initiation of the response under the condition that the subject has been instructed to respond as rapidly as possible.

It evaluates the processing speed of central nervous system (CNS) and coordination between the sensory and motor systems. Reaction time measurement includes the latency in sensory neural code traversing peripheral and central pathways, perceptive and cognitive processing, and a motor signal traversing both central and peripheral neuronal structures and finally the latency in the end effectors activation (i.e., muscle activation).

Pregnancy hormones are found to affect ART. Mehta R et. al. (2017) in her study on pregnant women demonstrated variation in reaction time to auditory and visual stimulus in all three trimesters when

compared with non pregnant women attributable to neuromodulatory effect of estrogen and progesterone and also to hCG.[1]

Preeclampsia, characterized by widespread endothelial damage and dysfunction, systemic toxicity, coagulation defects, and an increased systemic inflammatory response, poses some risk factors for hearing loss. Preeclampsia-eclampsia fits the definition of syndrome: a group of symptoms or pathologic signs that consistently occur together and represents one of the most important complications of pregnancy (5%-7% of low-risk pregnancies). Although the cause of preeclampsia remains unknown, evidence for it manifests early in pregnancy with covert pathophysiologic changes that gain momentum across gestation. Unless delivery supervenes, these changes ultimately result in multiorgan involvement with a clinical spectrum that range from barely noticeable to one of cataclysmic, pathophysiologic deterioration that can be life threatening for both the mother and the fetus. These adverse maternal and fetal effects develop simultaneously.

Pregnancy-induced hypertension (PIH) complicates about 6-10% of pregnancies. It is defined as Systolic blood pressure (SBP) more than 140 mmHg and diastolic blood pressure (DBP) more than 90 mmHg. It is classified as mild (SBP = 140-149 and DBP = 90-99 mmHg), moderate (SBP = 150-159 and DBP = 100-109 mmHg) and severe (SBP more than 160 and DBP more than 110 mmHg).[2]

Canadian Hypertension Society referred PIH to one of four conditions:

1. Pre-existing hypertension

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2. Gestational hypertension and Preeclampsia
3. Pre-existing hypertension plus superimposed gestational hypertension with proteinuria
4. Unclassifiable hypertension

Terms such as “pre-eclampsia,” “gestational hypertension,” “toxemia of pregnancy,” “proteinuric hypertension,” “preeclampsia,” “pregnancy-induced hypertension,” “organic hypertension,” “true pre-eclampsia,” “latent essential hypertension in pregnancy,” “chronic hypertension” and “transient hypertension in pregnancy” have been used, invariably being misused and interchanged[3]

Hypertensive pregnancies are found to cause cochlear damage, raised hearing threshold and permanent hearing loss which doesn't resolve after delivery. Preeclampsia as well as eclamptic women reported significant cognitive failures that are thought to reflect neurocognitive dysfunction as studied by Postma I.R.(2014)[4]

Fields J. et. al. (2017) in his study found women with a history of hypertensive pregnancy frequently reported subjective cognitive symptoms. [5]

We planned this study to assess auditory functions and subjective cognitive changes in PIH patients which can help early diagnosis and prevention of long term and post pregnancy morbidity which is usually not emphasized in antenatal checkups in the Gwalior district.

Material and methods

Study was conducted cross sectionally on pregnant females in 3rd trimester from Gajra Raja Medical college and Hospitals OPD and IPDs during from July 2018-July 2019.

Cases were Pregnancy induced Hypertensive Pregnant females in third trimester and controls were healthy normotensive pregnant females in third trimester.

Pregnant Females with any complication or previous history of chronic hypertension or in which PIH has advanced to eclampsia or Seizures were excluded.

Detailed obstetric history was taken for every case and control. General physical Examination was done to assess consciousness and awareness. Blood Pressure was recorded of each subject using Mercury Sphygmomanometer instrument. Urine albumin dipstick test was done on the spot.

Patients were divided into two groups and Auditory reaction time test were performed by every subject. Two Groups are:-

1. Normotensive pregnant female in 3rd trimester (NTP)
2. Pregnancy Induced Hypertensive female in 3rd trimester (PIH)

Auditory reaction time test were performed by every subject.

Procedure for recording auditory reaction time

The subjects were made to sit comfortably and the procedure was explained to them. The procedure was carried out in a sound proofroom with adequate light. The test was done using Cognifun RT software from laptop computer. The testing procedure was quite

simple, Non-invasive and harmless to the participants. A 1000 Hz beep sound was presented at random intervals to the participants ear through a headphone and the subject pressed the space bar of the system that is placed in front of them as per the given instruction.

The readings obtained were entered in Microsoft Excel 2010 data sheet in a computer and was analysed using GRAPHPAD PRISM Statistical Software. Descriptive Statistics of the data were presented as percentages, mean and Standard Deviation. Unpaired t tests and ANOVA were used to compare between groups. $P < 0.05$ was considered statistically significant. Pearson Correlation coefficient were assessed

Ethical considerations

Participation in the survey was purely voluntary and informed written consent was obtained from every participant. Approval from the Institutional Ethical Committee was obtained before the study.

Results

In this study we included 50 Pregnancy induced Hypertensive Pregnant Females (PIH) in the age group 20 to 38 years. Primiparous PIH group has age range 20 to 34 yrs (Mean 23.42 ± 3.31 yrs) Multiparous PIH group has age range 20 to 38 yrs (Mean 27.70 ± 3.24 yrs) along with age matched 50 control Normotensive Pregnant (NTP) female subjects of age group 20 to 36 yrs. Primiparous NTP group were of age range 20 to 30 yrs (Mean 22.80 ± 1.72 yrs) Multiparous NTP group were of age range 20 to 36 yrs (Mean 27.14 ± 2.16 yrs).

Cases were Pregnant females specifically with Pregnancy Induced Hypertension only which has not complicated to Eclampsia or Seizures in third trimester with BP $\geq 140/90$ mm Hg. Controls were Normotensive Pregnant Females in third trimester with BP $< 140/90$ mm Hg. Height of NTP (Mean 157.37 ± 2.24 cm) and PIH (Mean 157.24 ± 1.8 cm) were not significantly different.

Weight in PIH group averaged 68.20 ± 0.72 kg while in NTP group it was 63.42 ± 0.38 kg. There is significant difference (p value < 0.05) in weight of both the groups whether primiparous or multiparous.

Auditory Reaction Time in PIH group was 506.84 ± 112.62 ms and that in NTP group was 445.57 ± 87.32 ms. There was highly significant difference in the Auditory Reaction time values in group PIH and NTP with p value < 0.001 .

ART is found to be significantly raised in multiparous PIH group when compared to Primiparous PIH group (Primiparous PIH 492.90 ± 69.63 ms Multiparous PIH 508.17 ± 122.02 ms).

Significant linear correlation was found between values of SBP and DBP with ART. Pearson Correlation Coefficient between SBP and ART was 0.331 with p value 0.001. Pearson Correlation Coefficient between DBP and ART was 0.272 with p value 0.006. This correlation signifies that with increase SBP and DBP the values of ART are increasing in a linear fashion.

Table 1: Vital Data of PIH and NTP groups

Parameter	PIH		NTP		Total		p value
	Primi (n=20)	Multi (n=30)	Primi (n=20)	Multi (n=30)	PIH	NTP	
Age (Years)	23.42 ± 3.31	27.70 ± 3.24	22.80 ± 1.72	27.14 ± 2.16	25.17 ± 3.35	25.11 ± 2.17	0.12
Height (cm)	157.35 ± 0.88	156.40 ± 1.56	156.70 ± 2.52	157.10 ± 1.13	157.24 ± 2.24	157.37 ± 1.81	0.32
Weight (kg)	68.10 ± 0.28	69.41 ± 0.41	61.60 ± 0.22	65.40 ± 0.27	68.20 ± 0.72	63.42 ± 0.38	< 0.001

Table 2 : Blood Pressure in PIH and NTP groups

Blood Pressure	PIH (n=50)			NTP (n=50)			p value
	Primi-parous	Multi-parous	Total	Primi-parous	Multi-parous	Total	
SBP (mmHg)	156.80 ± 2.41	160.80 ± 0.13	158.70 ± 2.33	114.40 ± 1.25	116.40 ± 1.22	115.20 ± 1.12	< 0.0001
DBP (mmHg)	103.40 ± 1.25	106.40 ± 1.22	104.30 ± 1.46	70.80 ± 1.26	72.40 ± 0.96	71.20 ± 1.16	< 0.0001

Table 3: ART in PIH AND NTP groups

S.No.	ART	PIH (n=50)	NTP (n=50)
1.	Frequency	50	50
2.	Mean (msec)	506.84	445.57
3.	Std. Deviation	112.62	87.32
4.	P Value	< 0.001	

Table 4: ART in Primiparous and Multiparous PIH group

S.No.	ART	Primiparous	Multiparous
1.	Frequency	20	30
2.	Mean (msec)	492.90	508.17
3.	Std. Deviation	69.63	122.02
4.	t, df	t = 2.86 df = 48	
5.	P Value	0.006	

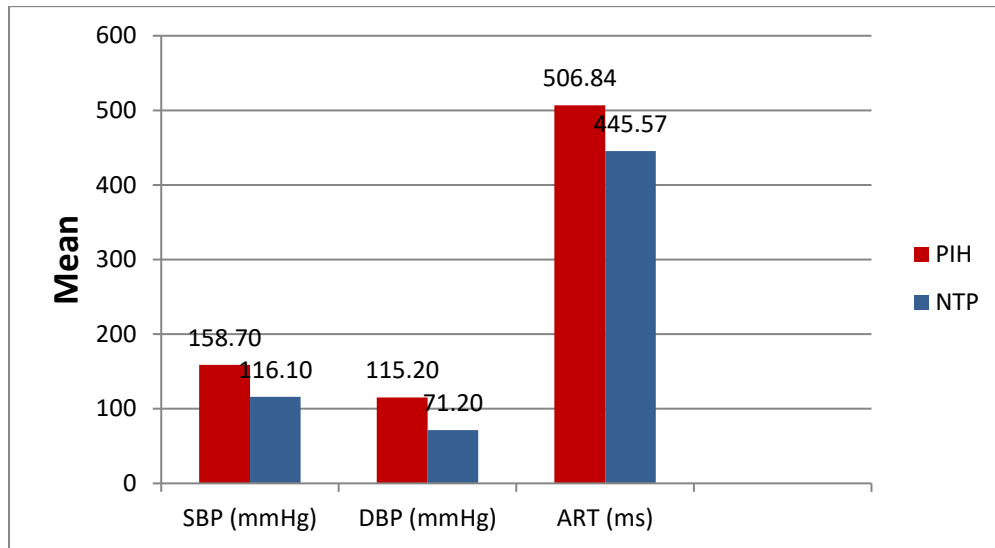


Fig. 1: Mean values of SBP & DBP and ART &VRT in both the groups

Table 5: Mean Values of SBP, DBP, ART and DBP with Correlation values

Parameter	Mean ± SD	SBP (Mean = 115.83 ± 1.22 mmHg) N = 100		DBP (Mean = 86.08 ± 0.87 mm Hg) N = 100	
		Pearson Correlation coefficient	p Value	Pearson Correlation coefficient	p Value
ART	469.09 ± 105.62 Milliseconds	0.331	0.001	0.272	0.006

Mean Values of SBP in subjects of both the groups N=100 was

115.83 ± 1.22 mm Hg. Mean Value of DBP in subjects of both the groups was 86.08 ± 0.87 mm Hg. Mean value of ART overall 100 subjects was 469.09 ± 105.62 ms.

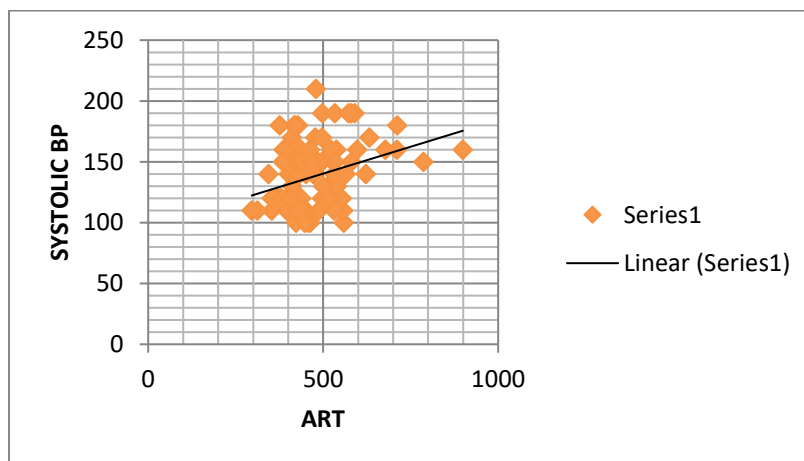


Fig. 2: Correlation of SBP with ART

The above scatter plot chart shows highly positive correlation between SBP and ART in both PIH and NTP. (Pearson correlation $R = 0.331$)

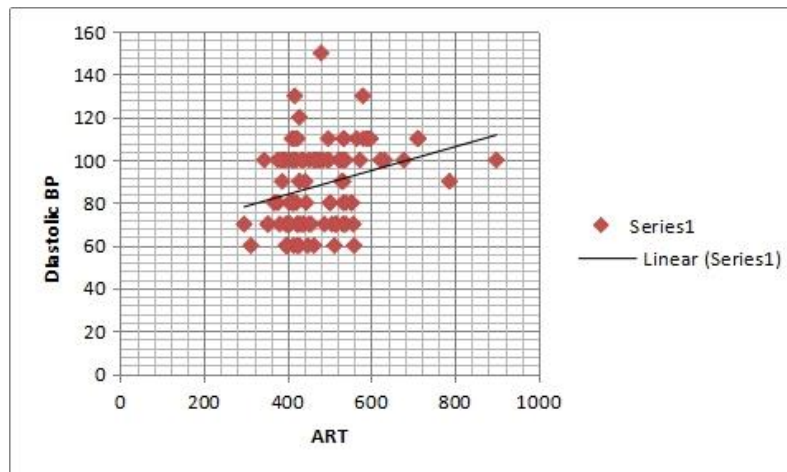


Fig. 3: Correlation of DBP with ART

The above scatter plot chart shows highly positive correlation between DBP and ART in both PIH and NTP. (Pearson correlation $R = 0.272$)

Discussion

Pregnancy Induced Hypertension (PIH) and Preeclampsia are leading direct cause of maternal and fetal morbidity and mortality worldwide with prevalence of 2–8% among pregnancies. Many a times it is undiagnosed and lands up in post pregnancy complications like hearing-visual impairments, chronic hypertension or cardiovascular compromises.

So the screening tests for complications at the time of diagnosis becomes a need for early detection and prevention of disease progression to end stage.

Reaction time (RT) is an index of processing ability of the central nervous system and nervous degenerative changes. Reaction time is a simple, non-invasive test and can be done easily without much expertise. [1]

This study has been undertaken to see whether Auditory Reaction Time (ART) can be useful to detect early complications of Pregnancy Induced Hypertension and/or Preeclampsia which can hamper post pregnancy outcomes.

In our study weight in PIH group was significantly (p value <0.05) different from NTP group whether primiparous or multiparous. Rebeloin their study concluded that the mean SBP/DBP (130/80 mm Hg) were significantly higher among overweight/obese women with BMI ≥ 25 kg/m² in the third trimesters. There was longitudinal linear regression model which showed that BMI was positively associated with prospective changes in SBP and DBP in pregnancies complicated with hypertension. [6]

Auditory Reaction Time in PIH group was significantly raised from that in NTP group with p value <0.001 . Our findings are agreeing with the conclusion made by Baylan et. al. and Atmaja et. al who studied otoacoustic emissions on preeclampsia subjects. They speculated that in patients with preeclampsia, endolymphatic hydrops developed after microvascular circulation deficiency which could be the reason for the loss of hearing at low frequencies. Pregnancy induced Hypertension can be considered responsible to cause microvascular changes in cochlea leading to auditory function impairments and prolongs the auditory reaction time. [7,8]

ART is found to be significantly raised in multiparous PIH group when compared to Primiparous PIH group (p value <0.05). This can be because of recurrent or prolonged or unresolved hypertensive state

in multiparous PIH subjects leading to worsening of pre-existing microvascular injury or cochlear damage. It is claimed by **Atmaja et. al and Baylan et. al.** that even if preeclampsia resolves after delivery, cochlear damage and permanent hearing loss remain unchanged in patients with preeclampsia.

A linear correlation has been found in values of ART with the values of SBP and DBP with significant Pearson correlation coefficient in our studies. It can be concluded that more the Blood pressure rises more will be delay in ART. Pearson Correlation Coefficient between SBP and ART was 0.331 with p value 0.001. Pearson Correlation Coefficient between DBP and ART was 0.272 with p value 0.006. This correlation signifies that with increase SBP and DBP the value of ART is increasing in a linear fashion. Therefore, it can be postulated that increase in Systolic and Diastolic B.P is a major factor responsible for increased values of ART in the subjects whether the subject is primiparous or multiparous. With the studies from evidences we can say that raised BP affects microvasculature and peripheral nervous system causing deleterious and unresolving effects on Auditory conduction pathways delaying the reaction time.

Aukeset. al. (2007) have reported cerebral white matter lesions in MRI study of preeclamptic women emphasizingly in white matter causing cognitive difficulties. [9]

Mielke M. et al. (2010) have found brain atrophies and white matter hyperintensities decades later Hypertensive pregnancies suggesting a lifelong impact of PIH or Preeclampsia on brain functions. They also confirmed cognitive failures in their subjects. [10]

Hypertensive state in general is found to cause delayed reaction time and cognitive performances as studied by Khode V. et al. (2013), Selvaa R. et al. (2017). [11,12]

Hypertension also increase hearing threshold as studied by Agarwal S. et al. (2013) and Caroline L. et al. (2014) [13,14]

Harrington F. et al. 2000 also have found altered cerebral metabolic process of cerebral blood flow in Hypertension. [15]

An additive effect of hormones estrogen and progesterone along with hypertensive state can be considered responsible for increased values of ART.

Estrogen is found to cause salt and water retention as is studied by Das A. (1997), Nene A. (2010), Kumar S. (2012), Pawar B. (2006), Bennel A. and Chavan B. (2017), Stachenled N. (2008). With salt

and water retention there is alteration of intracellular composition of brain cells which may be largely responsible for the diffuse alterations in brain function as is connoted by Pollock A. (1980). This can cause cerebral edema and altered neurotransmitter release. Progesterone is also found to affect the neuropsychological state of pregnant women especially during third trimester when the levels of Progesterone are highest.[16–21]

Henry and Rendall (2007) have concluded in their studies that Pregnant women can have subtle cognitive deficits. Parson et al. (2004), have studied that primiparous women suffer more of cognitive difficulties when compared to multiparous women. Buckwalter et al. (2001) concluded from his studies that these cognitive changes are due to high levels of progesterone especially in third trimester of pregnancy. [22–24]

Progesterone is also found responsible for peripartum and postpartum Maternity Blues in studies of Harris B. et al. (1980), Heidrich et al. (1994), Nott P. et al. (1976).[25–27]

In studies by De Groot et al. (2006) and Christensen et al. (2010) isolated effect of pregnancy on processing speed and poor cognitive performance during and after pregnancy is found. Hence during Pregnancy Reaction time is evidenced to be more than non pregnant state.[28,29]

Reaction time in patients of PIH is delayed due to additive effects of hormones estrogen and progesterone and microvascular changes, of PIH and leading to central and peripheral neurodegenerative changes developed long before development of clinically apparent symptoms (like hearing impairment, blindness, seizures etc). Along with this all these factors are also adversely affecting the cognitive abilities and hence delaying of the female.

Conclusion

This study, the first-ever conducted in the middle part of India, has revealed that a major proportion of Hypertensive Pregnant females have subtle and occult auditory-attention impairment. Routine antenatal checkups and early diagnosis of high risk pregnancies is sparsely done which is mainly because of unawareness among lower socioeconomic groups which forms major proportion of Indian Population.

Auditory Symptoms are usually not assessed as regular antenatal checkup.

In previous studies values of ART was found higher in Normal pregnancies when compared to non pregnant states. In this study we found ART was higher in Hypertensive pregnancies when compared to healthy pregnancies which is indicating that hypertensive pregnancies can have impact on auditory function. Raised ART also seen in patients with cognitive disabilities. It is opined that Hypertensive Pregnancies can impact cognitive abilities in the female which are also usually not assessed at the antenatal clinics.

It is suggested that ART test and otoscopic examination should also be included as a part of routine antenatal checkup.

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