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Original Article

Physiology Section

Influence of Age on Arterial Stiffness among Healthy Pregnant Women: A Cross-sectional Study

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ABSTRACT

Introduction: Normal pregnancy is associated with physiological cardiovascular system adaptations. Previous studies stated that physiological changes like arterial vasodilatation occurs for successful results for both mother and baby during pregnancy. Also, increased arterial stiffness during pregnancy causes several disorders, such as Pregnancy-Induced Hypertension (PIH) and foetal growth restriction.

Aim: To evaluate the influence of age on arterial stiffness among third-trimester healthy pregnant women using Pulse Wave Velocity (PWV).

Materials and Methods: This cross-sectional observational study was conducted at BLDE (University), Vijayapur, Karnataka, India, between April 2019 to July 2019. A total of 60 pregnant women were screened and 48 healthy pregnant women between 20-40 years with resting blood pressure <140/90 mmHg, non smokers and subjects not taking medications were included in the present study. The sample size was divided into four groups (group 1: 20-24 years; group 2: 25-29 years group 3: 30-34 years; and group 4: 35-40 years). Each group contained 12 participants and vascular stiffness parameters like brachial-ankle PWV (b-a PWV) and carotid-femoral PWV (c-f PWV) were evaluated. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software 16.0 version. Comparison between the mean values was done using Analysis of Variance (ANOVA) and Post-Hoc test (LSD) and correlation was assessed using Pearson's correlation test. The p-value ≤0.05 was considered significant.

Results: Mean and standard deviation of b-a PWV (group 1: 934.82±97.66; group 2: 970.27±101.92; group 3: 1077±112.20; group 4: 1563.2±143.47) c-f PWV (group 1: 574.78±62.81; group 2: 662.26±61.88; group 3: 769.88±65.51; group 4: 967.96±70.52) showed statistically significant (p<0.001) increase in both b-a PWV and c-f PWV with age among third trimester healthy pregnant women. Pearson's Correlation test showed significant positive correlation between b-a PWV (r=0.516, p<0.001) and c-f PWV (r=0.532, p<0.001) with age among third trimester pregnant women. The values of present study observed increase in both b-a PWV and c-f PWV with age.

Conclusion: Increased arterial stiffness with age among pregnant women, as assessed by PWV, predates the development of cardiovascular risk in women. This study may help obstetricians to reduce cardiovascular complications due to pregnancy in different age groups by suggesting regular physical activity, relaxation techniques and a healthy lifestyle to pregnant women in the early stage.

Keywords: Ageing, Cardiovascular risk, Pregnancy, Pulse wave velocity, Vascular stiffness

INTRODUCTION

In normal pregnancy, a significant rise in cardiac output and plasma volume is observed as a result of vascular vasodilatation. These cardiovascular alterations are essential for a healthy pregnancy and outcome [1]. Earlier studies have mentioned that increased PWV during pregnancy causes many diseases such as PIH and restricted foetal growth [2,3]. A decrease in vascular function with increasing age is considered a significant factor in ageing and is reflected in raised systolic blood pressure and decreased arterial compliance [4].

Increased PWV is an independent predictor of cardiovascular risk and organ failure [5]. It has been observed that from menarche to menopause, sex hormones in females fluctuate rhythmically during the menstrual cycle, and sex hormones increase considerably in pregnancy [6]. Estrogen and progesterone have an influence on arterial structure and function in females [6]. A study documented the initial effect of pregnancy reducing arterial stiffness [7]. The PWV can non invasively determine central arterial pressure and stiffness. PWV correlates more precisely with birth weight than Mean Arterial Pressure (MAP) among normotensive pregnancy, representing a maternal adaptation to pregnancy [8].

No studies showed effect of age on arterial stiffness among pregnant women. Studies need to explore the role of age on arterial stiffness during gestation. The current cross-sectional observational study aimed to evaluate the effects of the typical third trimester pregnancy on arterial stiffness among different age groups. This study might guide obstetricians to avoid age related cardiovascular complications in pregnancy.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in the Department of Physiology, Shri B.M. Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be University), Vijayapur, Karnataka, India between April 2019 to July 2019. The participants were recruited from the Obstetrics and Gynaecology Outpatient Department. This study was approved by the Institutional Ethical Committee (IEC) (BLDE(DU)/IEC/263/2017-18 dated 27th March 2018) as per the Indian Council of Medical Research (ICMR) guidelines 2006.

Sample size calculation: According to a previous study, the mean PWV (M./sec) was 6.84 m/s and standard deviation was 1.65 M./sec [9].

Formula used:

$$n=\frac{4\sigma^2}{L^2}$$

Where n is no. of samples and σ is the standard deviation.

The calculated sample size, when allowable error L=±1, was 11. To avoid the risk of dropouts, the sample size was considered as 12 in each group.

A total of 48 participants were divided into four groups with 12 participants in each group- (group 1: 20-24 years; group 2: 25-29 years; group 3: 30-34 years and group 4: 35-40 years).

Inclusion criteria: Healthy third trimester pregnant women with primipara, age ranging from 20-40 years with resting blood pressure <140/90 mmHg (average of three recordings), non smokers and participants not on medical treatment were included in the study.

Exclusion criteria: Subjects with systolic and diastolic blood pressure more than 140 and 90 mmHg, respectively, multiple pregnancies, diabetes mellitus, with a history of alcohol intake and tobacco consumption were excluded from the study.

Obtained written informed consent, and a detailed history was taken from all the participants. All the recordings were done from morning- 9 am to 11 am at room temperature; following supine rest for 10 minutes.

Study Procedure

Recording of physical and physiological variables: All the participants underwent recording of physical variables like height (cms)measured using a device (BIOCON™) mounted on the wall, weight (kg) measured using a weighing machine. Body Mass Index (BMI) (kg/m^2) was estimated from weight in Kilograms (Kg) divided by height in meters squared (m^2) and BSA (m^2) estimated from weight in Kilograms (Kg) and height in centimetres (cm) by using Dubois Body Surface Chart [10]. The physiological parameters like pulse rate in (Pulse Rate (PR); beats/min), Systolic Blood Pressure (SBP; mmHg), Diastolic Blood Pressure (DBP; mmHg), Pulse Pressure (PP; mmHg) and Mean Arterial Pressure (MAP; mmHg) were recorded by using a sphygmomanometer and following standard procedures.

Vascular function parameters: A non invasive automatic device was used to assess arterial stiffness, which was based on the Oscillometric method [11]. The instrument Periscope (Periscope, Genesis Medical Systems, India) uses two-channel electrocardiograph leads to record electrocardiogram and four blood pressure cuffs to record waves of arterial pressure [11]. Recordings of PWV were made in a lying position while blood pressure cuffs were enfolded on both upper limbs (arms) and lower limbs (above ankles), and electrocardiograph electrodes were applied on the medial side of ankles and anterior part of both wrists. The BP volume waveforms were measured by an oscillometric pressure sensor connected by BP cuffs. Volume pulse forms were determined from brachial and tibial arteries with the help of a plethysmographic sensor- recorded data for about 10 seconds. The data was stored in a computer for further analysis. As the device is fully automated and does not require any operator, the procedure is devoid of any operator bias. The device periscope is automatic; by displaying the results, the recording completes.

Pulse Wave Velocity

Brachial-ankle PWV (b-a PWV): This reflects the stiffness of the peripheral semi-muscular arteries and central elastic artery. Periscope uses Eectrocardiogram (ECG) recordings (Lead I and II) and brachial and tibial artery pressure waveforms to estimate brachial-ankle PWV. Calculated Pulse Transit Time (PTT) between the ankle and respective brachium as the time difference from the feet of the respective pulse wave, which originates from the R-wave (QRS complex) of ECG. The device calculated the distance between the sampling points of b-a PWV automatically based on the height of the participant.

To calculate the b-a PWV, the following formula is used.

$$baPWV=\frac{Lba}{PTTba}$$

Where b-a PWV=Brachial ankle PWV.

Lba=Distance between respective brachium and ankle.

PTTba=PTT between brachium and respective ankle was calculated as the time difference between the feet of respective pulse wave originated from R-wave (QRScomplex) of ECG [11].

The carotid-femoral PWV (c-f PWV): A measure of aortic stiffness was calculated by the composite b-a PWV found out by averaging left and right b-a PWV. Studies conducted elsewhere estimate the c-f PWV on the basis of equation (0.8333*Avg. b-a PWV-233.33) derived by regression analysis between b-a PWV and c-f PWV by using periscope [12].

STATISTICAL ANALYSIS

The data was expressed in the form of Mean±Standard Deviation (SD), and analysis was performed by incorporating the data in SPSS software (version 16.0). ANOVA followed by Post-Hoc test (LSD) was applied to find out the differences between the groups. Pearson's correlation test was applied to find out the correlation between brachial-ankle PWV, carotid-femoral PWV, with ageing. The p-value <0.05 was considered as significant.

RESULTS

Anthropometric characteristics of four age groups were analysed among third trimester pregnant women. No significant difference (p<0.05) among the groups in weight (p=0.806), height (p=0.06), BMI (p=0.791), and BSA (p=0.349) was found [Table/Fig 1].

Study showed no significant difference in PR (p=0.557) and DBP (p=0.14). ANOVA results also showed statistically significant difference (p>0.05) between age groups in systolic blood pressure (SBP; p<0.001), pulse pressure (PP; p<0.001) and mean arterial pressure (MAP; p=0.009). Post-hoc analysis showed significant increase in SBP, PP and MAP after the age of 34 years i.e. in the group 4 and did not show any significant changes in group 1 verses group 2, group 1 verses group 3 and group 2 verses group 3 [Table/Fig 2].

Mean and SD of both b-aPVW and c-fPVW from groups 1 to 4 among third trimester pregnant women depicted in [Table/Fig-3]. Post-hoc analysis showed a significant increase in b-a PWV (p<0.001) and c-f PVW (p<0.001) among group 4 versus group 1, 2 and 3; but did not show any significant changes in group 1 versus group 2, group 1 versus group 3 and group 2 versus group 3 [Table/Fig 3].

Pearson's Correlation between b-a PWV, c-f PWV and age did show a statistically significant moderate positive Correlation between b-a PWV (r=0.516, p<0.001) and c-f PWV (r=0.532, p<0.001) with age among third trimester pregnant women. It was observed that b-aPVW and c-f PWV increases with age [Table/Fig-4,5].

	Age groups (years)					
	Group 1	Group 2	Group 3	Group 4	ANOVA	
Parameters	20-24 years (n=12)	25-29 years (n=12)	30-34 years (n=12)	35-40 years (n=12)	F-value	p-value
Weight (Kg)	59.58±7.25	60±4.94	72.37±9.02	57±6.13	0.327	0.806
Height (cm)	153.3±7.9	156.75±3.64	150.25±5.81	152.83±3.78	2.759	0.06
BMI (kg/m^2)	25.33±2.53	24.42±3.4	25.35±2.72	25.35±1.90	0.348	0.791
BSA (m^2)	1.57±0.13	1.60±0.11	1.53±0.11	1.57±0.07	1.127	0.349

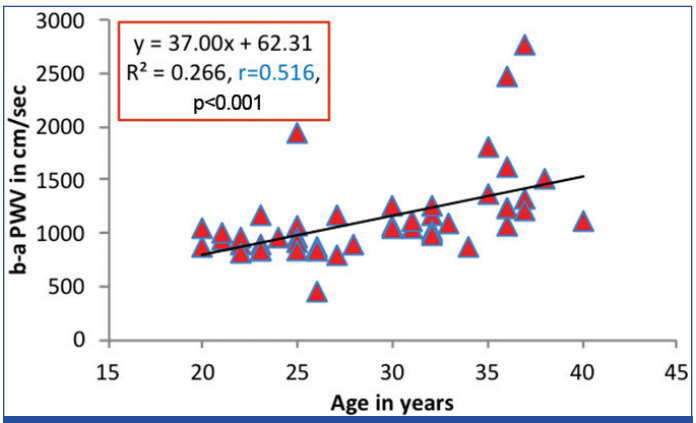
[Table/Fig-1]: Anthropometric characteristics of four age groups among third trimester pregnant women.
Data presented as Mean±SD; Values in the final column represent results of one-way analysis (ANOVA) among different age groups; Post-hoc comparisons were made between each group with LSD method; p<0.05 was considered significant. BMI: Body mass index and BSA: Body surface area

Parameters	Age groups (years)					
	Group 1	Group 2	Group 3	Group 4	ANOVA	
	20-24 years (n=12)	25-29 years (n=12)	30-34 years (n=12)	35-40 years (n=12)	F-value	p-value
PR (bpm)	82.14±10.34	87.1±11.25	86.14±9.24	86.4±4.94	0.701	0.557
SBP (mmHg)	118.17±12.43	115.67±13.75	121.58±8.01	139.92±15.57[1,2,3]	8.914	<0.001*
DBP (mmHg)	69.41±6.84	68.16±8.75	74.08±6.81	73.75±7.48	1.919	0.14
PP (mmHg)	48.75±9.94	47.5±9.22	47.5±5.16	66.16±12.5[1,2,3]	10.933	<0.001*
MAP (mmHg)	86.16±8.29	83.99±9.76	89.88±6.84	95.80±9.13[1,2,3]	4.353	0.009*

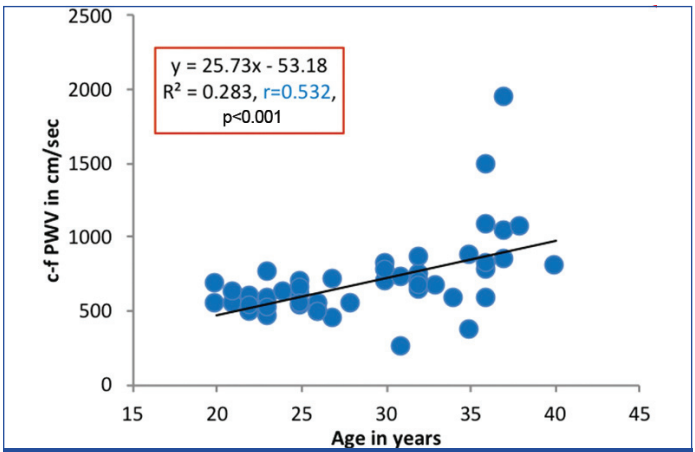
[Table/Fig-2]: Physiological characteristics of four age groups among third trimester pregnant women.
Data presented as Mean±SD. Values in the final column represent results of one-way analysis (ANOVA) among different age groups. Post-hoc comparisons were made between each group with LSD method. Superscripts 1, 2 and 3 on each group significantly differ from that group at p<0.05 level. PR: Pulse rate, PP: Pulse pressure, MAP: Mean arterial pressure

Parameters	Age groups (years)					
	Group 1	Group 2	Group 3	Group 4	ANOVA	
	20-24 years (n=12)	25-29 years (n=12)	30-34 years (n=12)	35-40 years (n=12)	F-value	p-value
b-a PWV, cm/sec	934.82±97.66	970.27±101.92	1077±112.20	1563.2±143.47[1,2,3]	9.175	<0.001*
c-f PWV, cm/sec	574.78±62.81	662.26±61.88	769.88±65.51	967.96±70.52[1,2,3]	8.152	<0.001*

[Table/Fig-3]: Vascular function parameters of four age groups among third trimester pregnant women.
Data presented as Mean±SD; Values in the final column represent results of one-way analysis (ANOVA) among different age groups. Post-hoc comparisons were made between each group with LSD method; Superscripts 1, 2 and 3 on each group significantly differ from that group at p<0.05 level; b-a PWV: brachial ankle pulse wave velocity, c-f PWV: carotid femoral pulse wave velocity



[Table/Fig-4]: Pearson's Correlation showing between brachial-ankle pulse wave velocity and ageing in third trimester pregnant women in four age groups.



[Table/Fig-5]: Pearson's Correlation showing relationship between carotid-femoral pulse wave velocity and ageing in third trimester pregnant women in four age groups.

DISCUSSION

The current study results from anthropometric parameters in all the age groups among third trimester pregnant women did not show any significant difference. A study on different age groups in normal individuals by Dey DK et al., showed variation in anthropometric parameters with age [13]. Results from the present study BP in all the age groups among third trimester pregnant women corroborate with the study of Franklin SS et al., [14]. The MAP and PP are the two components of arterial blood pressure, while MAP is steady and PP is a pulsatile component. Cardiac output and vascular resistance determine the MAP. The HR, early pulse wave reflection, large artery stiffness and left ventricular ejection influence the variation in pressure around the mean; this, in turn, determines the PP. Increased stiffness with increased resistance elevates SBP while DBP falls with increased stiffness and rises with increased resistance [15-19]. Therefore, with ageing changes in PP and MAP reflect severity of cardiovascular risk.

Age is considered a potent determinant of arterial stiffness, which leads to detrimental alterations in the cardiovascular system [20]. Arterial stiffness has become an increasingly important biomarker in the evaluation of Cardiovascular risk. The PWV is the major non invasive method for assessing the stiffness of arteries. The PWV reflects the elasticity of the segmental artery. Laurent S et al., states that, "cardiac contraction generates a pulse wave, which is propagated distally to the extremities and PWV is calculated as the distance travelled by the pulse wave divided by the time taken to travel the distance [21]. The present study showed increased arterial stiffness results suggesting the increased speed of the pulse wave in the arteries. The PWV can be measured in any arterial segment between two elastic and muscular arterial stiffness and is strongly correlated with c-f PWV, a measure of aortic stiffness [12]. Results from the present study showed an age-dependent increase in both b-a PWV and c-f PWV among third trimester pregnant women. According to O'Rourke MF and Yu SY and Blumenthal HT the possible mechanism for arterial stiffness in aged pregnant women might be elastin fatigue fracture, degradation, increased load on stiffer collagen fibres and calcification of media of arteries [22,23].

Limitation(s)

With more sample size, molecular study can be conducted to explain the behaviour of Vascular Endothelial Growth Factor (VEGF), Erythropoietin (EPO), Hypoxia-inducible factor 1 alpha (HIF 1α) and different vascular genes expression.

CONCLUSION(S)

The present study concludes that arterial stiffness increases with age in third trimester pregnant women. A better understanding of alterations in cardiovascular functions during normal gestation is critical to find out the disease's pathology. This study may serve as an eye-opener for obstetricians to reduce cardiovascular complications due to pregnancy in different age groups by suggesting regular physical activity, relaxation techniques and a healthy lifestyle to pregnant women in the early stage. In the future, molecular studies may help to reduce cardiovascular risk among late pregnancies by targeting particular genes responsible for arterial stiffness.

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