ABSTRACT

Background: Hypertensive disease in pregnancy continues to be one of the leading cause of maternal death. Pregnancy induced hypertension (PIH) is said to be accompanied by several cardiovascular pathophysiological changes including increases in arterial stiffness. Pulse wave velocity (PWV) is the method for measuring arterial stiffness. Both the pulse wave form and the velocity are said to change in PIH. However, studies documenting these characteristics of PWV have mainly been in the Caucasian population.

Aims & Objectives: To establish the characteristics of PWV in normotensive and hypertensive pregnant women at the UTH in Lusaka, Zambia.

Methodology: This cross-sectional study comprised of 26 systematically selected pregnant women between the ages 18-45 years old who met the criteria. A structured interview was used to collect socio demographic data. Anthropometric measurements were taken. After a 15 minute rest, peripheral systolic and diastolic BP were measured. The PWV measurement involved applying non-invasive piezoelectric sensors over the skin after palpating for the carotid artery on the neck and the radial artery on the wrist (carotid-radial segment C-R PWV). Using IBM® SPSS® version 20.0 analyses were made using mann-whitney and spearman correlation tests. A 95% confidence interval (CI) and P-value of < .05 were set.

Results: Quality recordings were obtained from C-R PWV process (p=.05). There were significant increase in AP indicating an increase in pressure difference from the systolic shoulder to its peak (p=.05). There is also a significant increase in Aix indicating an increase in arterial stiffness (p=.05). This is further supported by a significant difference in PWV.

Conclusion: Distinct differences were seen in the waveform and PWV amongst individuals with PIH. This supports the vascular changes said to take place in PIH. Thus, PWV can be used as a measure for arterial stiffness.

Keywords: Pulse wave velocity (PWV), pregnant women, hypertension

1.0 INTRODUCTION

Pulse wave velocity (PWV), the speed at which the pulse wave travels on an arterial segment, is considered the “gold standard” in the measurement of arterial stiffness (1). It is described as a simple, non-invasive and reproducible method of measurement (2). It has also been described as a strong predictor for future cardiovascular (CV) events (3).

The pulse wave carries information on how blood is propagated along an arterial segment and not only systolic and diastolic pressures as measured by a sphygmomanometer. Both
the pulse wave form and the pulse wave velocity are definitive of vascular health. Determinants of the wave form are ‘ejection pattern of the left ventricle, the mechanical properties of the arterial system, and the peripheral vascular resistance’ (4). The pulse wave velocity can be measured between the carotid radial arterial system it spans called carotid-radial PWV (crPWV). Carotid-radial PWV is said to be a measure of muscular artery stiffness (5).

Several hemodynamic changes have been reported in pregnancy due to several physiological and/or pathophysiological processes that occur at the different stages of pregnancy. Among the pathophysiological processes reported in pregnancy induced hypertension (PIH) is endothelial dysfunction which causes increased arterial stiffness. This is said to be caused mainly by the release of toxic substances that consequently inhibit the bioavailability of nitric oxide which is a vasodilator (6,7,8,9,10). Indeed PWV is said to increase significantly in women with PIH when compared to normotensive pregnant controls (13). However, these findings have been mostly in the Caucasian population. Data in African women is lacking.

Pregnancy induced hypertension (PIH) is very common in the African population. Its prevalence in South Africa was reported as 21.6% in 2012 (11) and at the University Teaching Hospital (UTH) Lusaka, it was estimated to be around 12% in 2012 (personal communication, UTH Dept. of Obstetrics and Gynaecology). Women of African descent are said to be more likely to develop preeclampsia than those of the Caucasian population (13). This has been attributed to genetic factors (13).

1.1 Pulse Wave Form and Velocity

A typical pulse waveform contains an augmentation pressure (AP) which represents the pressure from systolic shoulder to the peak. Its index, (augmentation index (Aix)), is calculated as the difference between $P_2$ and $P_1$ expressed as percentage of the pulse pressure.

These indices are all markers in cardiovascular measurements. However, these have not been documented in pregnant women of African descent. This study seeks to explore this aspect.

1.2 Differences in arterial pulse wave propagation

The pulse waveform’s shape is said to be a result of the summation of a direct wave and a reflected wave, both of which propagate along the arterial tree. The shape and magnitude of these waves are able to change as the characteristics in the structure of the arteries change. The arrival of the reflected wave is dependent on the compliance of the arterial wall. In a compliant elastic artery the reflective wave is said to travel rather slowly and returns in late systole (1). However, in a stiff artery, typical of hypertensive disorders, the reflected wave is said to travel faster resulting in a greater amplification of the peak (augmentation pressure) and returns in early systole consequently increasing the aortic pressure (1). This has implications on approaches to treatment modalities. While this has been noted in both primary and secondary hypertension, very little literature exists on the waveform and magnitude of PWV in PIH.
2.0 MATERIAL AND METHODS

This cross sectional study included all pregnant women between the age of 18-45 years presenting to the UTH department of obstetrics and gynaecology for a routine antenatal clinic visit during the study period (April to June 2014) who met the eligibility criteria and gave consent to participate. Excluded were pregnant women younger than 18 years and older than 45 years or women with chronic hypertension, diabetes mellitus and any known cardiovascular pathology.

2.1 Socio-Demographic Data

All consenting participants were interviewed to obtain socio-demographic data and health information such as maternal age, marital status, gestational age, smoking status or exposure to tobacco smoke, history of diabetes mellitus or use of either hypoglycaemic agents, history of hypertension or use of anti-hypertensive medication, alcohol consumption, physical exercise, family history, history of other cardiovascular conditions and/or use of other medications.

2.2 Anthropometric Measurements

Body height was measured to the nearest 0.1cm using the Seca Brand 214 Portable Stadiometer (Seca gmbh & Co. kg Humburg, German). Participants were asked to remove their foot and head gear and with their heels against the back board looking ahead, measurements were taken. Weight was measured to the nearest 0.1kg using the Heine Portable Professional Adult Scale 737 (Seca gmbh & Co. kg Humburg, German). Participants were again asked to stand still with their face forward, and arms on the sides of the body. The length from the carotid artery (neck) to the radial artery recording sites was measured using a Figure-Finder tape measure.

2.3 Pulse Wave Velocity Measurements

After a 15 minute rest, peripheral systolic and diastolic BP was measured three times on the right arm whilst seated using an Omron M6 Comfort automatic BP monitor. The last two BP measurements were then averaged. Measurements were taken at 3 minute intervals. Participants were then asked to lie in the left lateral position to avoid vena cava compression by the uterus for another period of rest of 10 minutes. The Complior analyse was utilised to measure PWV. The PWV measurement involved applying non-invasive piezoelectric sensors over the skin after palpating for the carotid artery on the neck and the radial artery on the wrist. Other information measured with this software included: the augmentation index (Aix), a composite measure of systemic arterial stiffness, central systolic blood pressure (CSBP), central diastolic blood pressure (CDBP), central pulse pressure (CPP) and mean central arterial blood pressure (cMAP). During measurement, the women were requested not to move or speak. All measurements were taken by the same observers for all participants.

3.0 RESULTS

3.1 Anthropometric Measurements

A total of 26 women participated in this study. Of these, 14 were normotensive, 12 were newly diagnosed hypertensive participants.

Both groups recorded similar age ranges with means of 27 and 31 years for the normotensive and hypertensive participants respectively. The mean gestational age was
also similar in all blood pressure groups. Details of these characteristics are outlined in table 1.

### Table 1. Baseline characteristics of study groups

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (NTN) n=14</th>
<th>Hypertensive (HTN) n=12</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (yrs)</td>
<td>27 ± 6</td>
<td>31 ± 5</td>
<td>.14</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>26 ± 12</td>
<td>29 ± 7</td>
<td>.90</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>72 ± 15</td>
<td>77 ± 15</td>
<td>.65</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>164 ± 8</td>
<td>154 ± 32</td>
<td>.60</td>
</tr>
</tbody>
</table>

Values are given as means ± standard deviation. Asymptotic significances displayed across all study groups. The significance level is .05.

### 3.2 Blood Pressure

Table 2 shows an aggregation of both peripheral and central blood pressure results. Peripheral BPs recorded a mean of 93/59 amongst the normotensives and 124/78 amongst hypertensive participants.

### Table 2. Blood pressure

<table>
<thead>
<tr>
<th></th>
<th>NTN</th>
<th>HTN</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bSBP (mmHg)</td>
<td>93 ±9</td>
<td>124 ± 18</td>
<td>.00*</td>
</tr>
<tr>
<td>bDBP (mmHg)</td>
<td>59± 8</td>
<td>78 ± 10</td>
<td>.00*</td>
</tr>
<tr>
<td>bPP (mmHg)</td>
<td>34± 6</td>
<td>46±12</td>
<td>.00*</td>
</tr>
<tr>
<td>bMAP (mmHg)</td>
<td>70± 8</td>
<td>93±12</td>
<td>.00*</td>
</tr>
<tr>
<td>Carotid –Radial (C-R) measurements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cSBP (mmHg)</td>
<td>86 ± 10</td>
<td>119 ± 18</td>
<td>.00*</td>
</tr>
<tr>
<td>cDBP (mmHg)</td>
<td>59 ± 8</td>
<td>78 ± 10</td>
<td>.00*</td>
</tr>
<tr>
<td>cMAP (mmHg)</td>
<td>68 ± 7</td>
<td>90 ± 13</td>
<td>.00*</td>
</tr>
</tbody>
</table>
Mean central BPs from C-R recordings were 86/59 mmHg amongst the normotensive participants while the hypertensive participants recorded mean central BPs of 119/78 mmHg which were significantly higher ($P < .01$). Table 3 shows recordings made for augmentation pressures and PWVs.

### 3.3 PWV Measurements

<table>
<thead>
<tr>
<th></th>
<th>NTN</th>
<th>HTN</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>crPWV (m/sec)</td>
<td>9 ± 4</td>
<td>13 ± 7</td>
<td>.04*</td>
</tr>
<tr>
<td>AP (mmHg)</td>
<td>4 ± 5</td>
<td>9 ± 8</td>
<td>.05*</td>
</tr>
<tr>
<td>Aix (%)</td>
<td>1 ± 22</td>
<td>16 ± 23</td>
<td>.03*</td>
</tr>
</tbody>
</table>

AP = augmentation pressure, Aix = augmentation index, PWV = pulse wave velocity. Values are given as means ± standard deviation. The significance level is .05. Mann-whitney u test was used. * shows significant difference.

### 3.4 Augmentation Pressure

With the crPWV measurements, normotensives recorded 4 ± 5 mmHg and hypertensive participants, 9 ± 8 mmHg.

### 3.5 Augmentation Index

For Aix, normotensive participants recorded 1 ± 22% and amongst the hypertensive participants, 16 ± 23%.

Significant differences were recorded for the AP and Aix ($P = .05, .03$ respectively).

### 3.6 Pulse Waveform

Figure 1. A recording of pulse waveform for normotensive participants;
The Tsys period was completed before the T1 period elapsed. Thus consequently P2 preceded P1.

Figure 2. A recording of pulse waveform for hypertensive participants;
LVET= left ventricular ejection time, DT= diastolic time, P1= first systolic peak, P2=second systolic peak

T1 period was completed before the Tsys period elapsed. Consequently P1 preceded P2. The return of the reflected wave occurred in early systole causing an elevation in the systolic pressure and consequently augmentation pressure.

Normotensive participant showed that Tsys (the timing of the systolic wave) period was completed before the T1 period elapsed (timing of the reflected wave). This translates that the reflected wave arrived in late systole (type C wave). However for hypertensive participants T1 period was completed before the Tsys period elapsed translating that the reflected wave came early in systole (type A). AP was larger in the hypertensive participant as a result of an increased systolic pressure.

The relationship between central and peripheral diastolic pressures and crPWV was investigated using Spearman’s correlation. There was a strong positive correlation between central and peripheral diastolic pressures and crPWV rho=0.626 and 0.590 respectively at a significance level of .01 (n=26).

A moderate positive correlation was seen between central and peripheral systolic pressures and crPWV rho=.396 and .423 respectively at significance of .05 level with shared variance of 15.68% and 17.89% respectively.

4.0 DISCUSSION

4.1 Demographical Differences

The age groups of all consenting participants showed no significant difference and thus were comparable (P=.14). This is notable as age is a determinant that is said to cause increases in arterial stiffness and consequently BP. Arterial stiffness does increase with age (14). This is attributed amongst others to the decrease in nitric oxide synthesis and elastin fragmentation and degradation leading to the loading of collagen fibers in the arterial tree.

All the participants were of comparable heights and weights. The height of an individual defines the distance travelled by blood to particular reflection points. ‘The shorter the distance travelled, the greater the amplitude of the reflected pulse wave’ (15). Increases in fatty deposits (plaques) on the arteries leads to arterial stiffening and narrows blood vessels compromising its flow. Thus weight and height can be confounders to arterial stiffness. However, because there were no significant differences amongst these categories, participant groups were comparable.

4.2 Blood Pressure

This study joins many other studies in establishing significant differences in peripheral and central blood pressures amongst normotensives when compared to hypertensive participants. These increases in blood pressure are said to be due to the structural changes that occur on the vascular lining of these vessels. This suggests that a relationship exists between blood pressure and PWV regardless of whether the arterial stiffness is a cause or consequence of blood pressure.

4.3 Augmentation Index (Aix)
Aix, a surrogate measure of the reflected pulse wave, is an important cardiovascular measure because it is able to distinguish between the effects of different vasoactive medications which may not be appreciated using PWV (16). A significant difference was found in Aix between hypertensive pregnant women and normotensive participants. This suggests that significant arterial stiffness was exhibited and consequently the reflected wave returned before ventricular ejection in hypertensive participants.

4.4 Pulse Wave Velocity (PWV) Measurements

This study has attempted to establish mean PWV values in normotensive and hypertensive pregnant women of African descent. crPWV was significantly different between these two groups. This suggests that the proposed endothelial dysfunction has occurred along the carotid-radial segment which spans the subclavian, brachial, and radial arteries (17), resulting in significant arterial stiffness. This increased stiffening resulting in a decrease in diameter of the vessel, causes increases in blood flow and consequently blood pressure. Central blood pressures, often described as a better predictor of cardiovascular events, and peripheral blood pressures correlated positively with PWV (cSBP; rho=.396, cDBP; rho=.626, bSBP; rho=.423, bDBP; rho=.590) That is, hypertensive participants had a higher PWV than normotensive participants.

With the reduction in systemic vascular resistance (SVR) that occurs in the normal adaptation of pregnancy, a reduction in both systolic and diastolic blood pressures is expected with diastolic pressure being more reduced (18). This was evidenced by the strong positive correlation seen between crPWV and diastolic blood pressure (rho=.626).

The waveforms generated were typical to those described in literature (13,6,19). A C-type wave was generated in normotensive participants. This wave depicts the return of the reflected wave in late systole after ventricular ejection has ceased, characteristic in young adults (>30 years) (1,20). In hypertensive pregnant individuals, either an A or B type wave is generated. In these waveforms, the reflected wave arrives early in systole during ventricular ejection, and the timing of the reflected wave (t1) is shorter than the systolic wave (t2) (1,20). Amplification of the systolic pressure is also seen in these participants. This can be seen by an increase in the AP. Results show a hypertensive participant with a type A wave because their Aix is above 12% (Aix = 31.04%).

In more severe cases of PIH, increased arterial stiffness, increased endothelial dysfunction resulting in proteinuria and increased blood pressures are expected. Amongst the participants investigated, 11 of the 12 hypertensive participants had 0- trace amounts of protein in their urine. Hence comparisons could not be made between arterial stiffness and proteinuria.

4.5 Limitations

Characteristics of PWV were not measured longitudinally throughout pregnancy and after delivery, to assess the persistence of arterial stiffness. Variations are seen in aortic stiffness throughout the gestational period with its lowest in the second trimester and its' highest in the third during normal pregnancy (6). This change in arterial stiffness is due to the remodelling of blood vessels that occurs in pregnancy resulting in increases in cardiac output, plasma volume and decrease in vascular resistance. This remodelling ceases once birth occurs.
5.0 CONCLUSION

Quality results were obtained from crPWV measurements. Arterial stiffness increases significantly in PIH (crPWV). This has been attributed to endothelium dysfunction that occurs in PIH. There are distinct differences in the pattern of the waveform in PIH. In normotensive individuals the reflected wave returns to the ascending aorta after ventricular ejection. In contrast, hypertensive individuals had their reflected wave returning during ventricular ejection giving rise to the systolic pressure and consequently an increase in the augmentation pressure. With the distinct vascular changes that occur in PIH more studies need to be conducted using PWV as an early predictor of women at risk of developing PIH and as a factor for initiating and monitoring treatment.

ETHICAL APPROVAL

All authors hereby declare that the protocol was approved by ERES Converge IRB.

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