PULSE WAVE VELOCITY IN NORMOTENSIVE AND HYPERTENSIVE PREGNANT WOMEN AT UNIVERSITY TEACHING HOSPITAL (UTH), LUSAKA, ZAMBIA.

By

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A dissertation submitted to the University of Zambia in partial fulfilment of the requirements of the degree of Master of Science in Human Physiology.

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DECLARATION

I HEREBY DECLARE THAT THIS DISSERTATION HEREIN PRESENTED FOR THE DEGREE OF MASTER OF SCIENCE IN HUMAN PHYSIOLOGY HAS NOT BEEN PREVIOUSLY SUBMITTED EITHER WHOLLY OR IN PART FOR ANY OTHER DEGREE AT THIS OR ANY OTHER UNIVERSITY NOR IS IT BEING CURRENTLY SUBMITTED FOR ANY OTHER DEGREE.

SIGNED: ……..

LONGA KALUBA

CERTIFICATE OF APPROVAL

This dissertation by **Longa Kaluba** has been approved as fulfilling the requirements for the award of the degree of Master of Science in Human Physiology by the University of Zambia.

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Supervisor Signature

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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 34 systemically selected pregnant women between the ages 18-45 years old who met the criteria. A structured interview was used to collect socio demographic data. Participants' weights and heights were then measured. After a 15 minute rest, peripheral systolic and diastolic BP were measured using an Omron M6 comfort automatic BP monitor. 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); and for the carotid-femoral segment (C-F PWV) palpation was donefor the carotid artery on the neck and the femoral artery on the inner thigh. Using IBM® SPSS® version 20.0, analyses included: kruskal-wallis, mann- whitney tests and spearman correlation tests. A 95% confidence interval (CI) and *P*-value of < 0.05 were set.

Results: Quality recordings were obtained from C-R PWV process ($p=0.041$) between normotensive and hypertensive participants. There were significant increase in AP indicating an increase in pressure difference from the systolic shoulder to its peak ($p=0.046$). There is also a significant increase in Aix indicating an increase in arterial stiffness ($p=0.031$). This is further supported by a significant difference in PWV. Results from the C-F procedure experienced severe anatomical influences of the pregnant uterus and should therefore be ignored.

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 and in the screening of PIH and possible treatment.

DEDICATION

This dissertation is dedicated to:

My darling daughter,

My life is more meaningful with you in it.

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I would like to give thanks the Lord God Almighty for allowing me to see this project through.

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CHAPTER ONE
INTRODUCTION
1.1 BACKGROUND

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 (Complior analyse operator manual, 2013). It is described as a simple, non-invasive and reproducible method (Cieslik-Guerra, et al., 2013). It has also been described as a strong predictor for future cardiovascular (CV) events (Vlachopoulos, et al., 2010).

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' (Ohal & Vaidya, 2012). The pulse wave velocity can be measured between the carotid radial arterial system it spans called carotid-radial PWV (crPWV); and carotid femoral arterial system called carotid-femoral PWV (cfPWV).The carotid-femoral PWV is said to be a measure of aortic stiffness whereas carotid-radial PWV, a measure of muscular artery stiffness (Mitchell, et al., 2010).

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 leads to increased arterial stiffness. This is said to be caused mainly by the release of toxic substances that consequently inhibits the bioavailability of nitric oxide which is a vasodilator (Steinberg, et al., 1996, Steinberg, et al., 2000, Savvidou, et al., 2003, Kaihura, et al., 2009, Jin, et al., 2007).

Pregnancy induced hypertension (PIH) is very common in the African population. Its prevalence in South Africa was reported at 21.6%from 2011-2012 (Moodley, 1998) and at the University Teaching Hospital (UTH), 12% in 2012(personal communication, UTH Dept. of Obstetrics and Gynaecology).

PIH is defined as gestational hypertension with a blood pressure (BP) of equal to or greater than140/90mmHg which usually develops after 20 weeks of gestation and resolves within 42 days post-partum with no proteinuria; while preeclampsia (PE)is described as BP of equal to or greater than160/110mmHgwith proteinuria≥ 2g/24h which usually develops after the 20th week of gestation (National High Blood Pressure Education Program Working Group in High Blood Pressure in Pregnancy, 2000).Studies have shown that women of African descent are more likely to develop PE than those of the Caucasian population. This has been attributed to genetic factors (Khalil, et al., 2009).

PWV is said to increase significantly in women with PIH when compared to normotensive pregnant controls (Kaihura, et al., 2009). However, these findings have all been in the Caucasian population.

i. Pulse Wave Form and Velocity

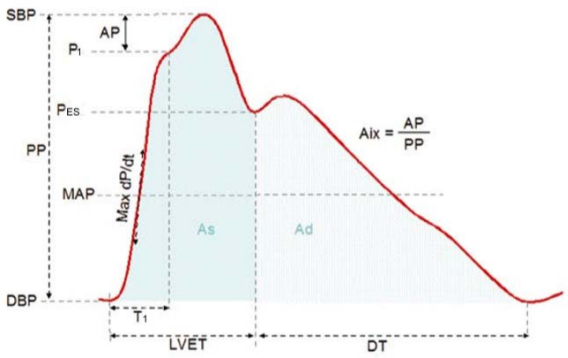

Figure 1 Typical pulse wave form (Complior analyse, n.d.); AP= Augmentation Pressure, Aix = augmentation index, P1=first systolic peak, PES = end systolic blood pressure, MAP= mean arterial pressure, LVET= left ventricular ejection time, DT= diastolic time T1= timing of reflected wave, SBP= systolic blood pressure, DBP= diastolic blood pressure, PP= pulse pressure.

The above diagram (Figure 1) shows a typical pulse waveform. The augmentation pressure (AP) represents the pressure from systolic shoulder to the peak. Its index, (augmentation index (Aix)), is calculated as the difference between P2 and P1expressed as percentage of the pulse pressure. The indices described 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.

ii. Differences in arterial pulse wave propagation

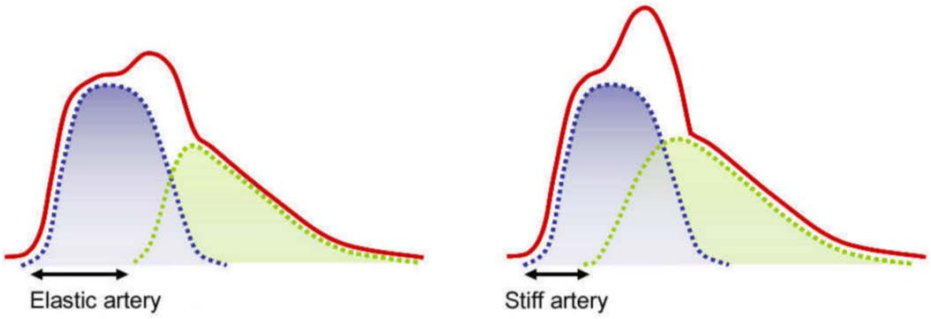

Figure 2 Wave propagation ***(Complior analyse operator manual, 2013)***

The pulse waveform's shape is a result of the summation of a direct (blue coloured wave) and reflected wave (green coloured wave), both of which propagate along the arterial tree. Both of these waves are able to change shape as the characteristics in the structure of the arteries change. 'Aortic stiffness affects the arrival of the reflective wave' (Complior analyse operator manual, 2013). In an elastic aorta, the reflective wave will travel slower and return in late systole (Complior analyse operator manual, 2013).

However, in a stiff artery typical in hypertensive disorders, the reflected wave will travel faster resulting in a greater amplification of the peak (augmentation pressure) and consequently an increase in the aortic pressure (Complior analyse operator manual, 2013).This has implications on approaches to treatment modalities.

While this is noted in both primary and secondary hypertension, there is very little literature on the waveform and magnitude of PWV in PIH.

1.2 STATEMENT OF THE PROBLEM

There are very few pathophysiological studies done on the pulse wave form in PIH, a serious problem in maternal health. PIH is said to be accompanied by several cardiovascular changes including increases in arterial stiffness. However, studies documented have mainly been in the Caucasian population even though those of African descent are said to be more predisposed to PIH. This study endeavoured to

determine the methodology for recording of PWV, characterising the waveform and documenting the magnitude of PWV in women of African descent with PIH.

1.3 JUSTIFICATION OF STUDY

Arterial stiffness is a marker for most hypertensive disorders. However, most studies have shown that arterial stiffness either remains unchanged or decreases amongst pregnant women when compared with non-pregnant women but increases significantly in hypertensive women when compared to normotensive pregnant women. However, little is known of the characteristics of PWV in both normotensive and hypertensive pregnant women typically in the black population. Whether these differences are significantly different between the whites and blacks or whether an index can be used to identify those who are at risk of PIH still remains to be known. However, these questions can only be answered once the characteristics and rate of the pulse waves are identified and thus the purpose of the study.

1.4 GENERAL OBJECTIVE

To determine the characteristics of PWV amongst normotensive and hypertensive pregnant women at UTH, Lusaka, Zambia.

1.5 RESEARCH QUESTION

What are the characteristics of PWV in normotensive and hypertensive pregnant women at University Teaching Hospital (UTH) in Lusaka, Zambia?

1.6 SPECIFIC OBJECTIVES

a) To determine PWV in normotensive and hypertensive pregnant women.
b) To determine the characteristics of the pulse wave form amongst normotensive and hypertensive pregnant women.

CHAPTER TWO
LITERATURE REVIEW
2.1 WAVEFORM CHARACTERISTICS

Differences in aortic stiffness are seen between normotensive and hypertensive pregnant women (Kaihura, et al., 2009). Coincidently, their waveform characteristics are also evident. Normally the reflected wave returns to the ascending aorta after ventricular ejection. Thus increases in the aortic pressure caused by the reflected wave occur in diastole and not systole. This results in increases in diastolic pressure and is said to be physiologically responsible for the increases noted in coronary blood flow to the myocardium during diastole without any increase in the left ventricular afterload. In PIH the pulse wave form is said to travel more rapidly along the arterial tree with its reflected wave returning during ventricular ejection (Nichols, et al., 2011). This causes an increase in the systolic pressure (seen by the amplification of the systolic peak), increased augmentation pressure (AP), and an increased augmentation index (Aix) (Complior analyse operator manual, 2013) and consequently the ventricular afterload (Nichols, et al., 2011).

The aortic pressure waves have been classified into four types namely Type A,B,C and D according to the timing and amplitude of the reflected wave from peripheral sites. Type A and B occur when the systolic peak (P2) occurs in late systole after a well-defined inflection point with differences in the degree of the Aix. In type A the Aix is greater than 12% whereas in type B, it's between 0-12%. Type C wave occurs when the inflection point occurs after the systolic peak whereas in type D no inflection point is measured because the reflected wave arrives in early systole and merges with the incident wave (Nichols, et al., 2011). Types A and B are characteristic in hypertensive individuals and those >12 years old. Type C is characteristic for normotensive individuals whereas type D for individuals above the age of 65 (Nichols, et al., 2011).

Aix, a measure of systemic arterial stiffness, is influenced by heart rate (HR) and any other changes in both cardiac and vascular function which can be influenced by drugs for example (Wilkinson, et al., 2000). Aix can be controlled at a heart rate of 75bpm (Aix-75) because of the linear relationship that exists between heart rate and Aix (Wilkinson, et al., 2000).

Women with PE have been reported to have a slower HR (overall PE p=0.002) and longer heart cycle (p=0.001), which has been attributed to the longer duration of diastole rather than the ejection duration time (Kaihura, et al., 2009).

There have been contrasting results regarding the relationship between AP, Aix and PWVs. Khalil et al, 2009 reported no significant difference in AP and Aix between Afrocarribean normotenisve and Caucasian normotensive women when confounders for arterial stiffness namely age, ethnicity, parity, smoking, and BMI were controlled for.

Furthermore, no significant differences in Aix-75 were seen between the Afrocarribean and Caucasian normotensive groups as well after correction for the differences in BMI (27.70 vs. 26.37; P=0.004) and nullparity (39.4% vs. 50.4%; P=0.024) were made. Despite this, Afrocarribean women were said to be still more predisposed to PE when compared to Caucasians (Khalil, et al., 2009).

These findings are supported by Kaihura et.al. who also reported no significant differences in the Aix between PE and non PE groups (Kaihura, et al., 2009). However other studies have suggested an elevated Aix in women with established PE (Robb, et al., 2009), (Spasojevic, et al., 2009), (Khalil, et al., 2009), (Ronnback, et al., 2005). Furthermore, increases have also been seen in peripheral pulse pressure, a valuable surrogate measurement of arterial stiffness (Kaihura, et al., 2009).

2.2 PATHOPHYSIOLOGY OF PIH

Significant endothelial dysfunction has been described in PIH. The dysfunction is said to be due to reduced blood flow to the placenta (Guyton & Hall, 2006). This ischemia of the placenta causes the release of toxic substances such as soluble Fms tyrosine kinase 1 (sFLt1) (Karumanchi & Lindheimer, 2008) and soluble endoglin (Levine, et al., 2006). These consequently cause dysfunction of vascular endothelial cells throughout the body including the blood vessels of the kidneys. Endothelial dysfunction is also said to decrease the release of nitric oxide and other vasodilator substances, causing relative vasoconstriction, decreased rate of fluid filtration from the glomeruli into the renal tubules, impaired renal pressure natriuresis, and thus development of hypertension.

The reduced blood flow to the kidneys also results in a decrease in the colloid osmotic pressure and increased vascular permeability thus loss of protein and fluid (Guyton & Hall, 2006).

'These 'nonhypertensive' complications that follow pre-eclampsia can be life-threatening even when blood pressure elevations are quite mild' (National High Blood Pressure Education Program Working Group in High Blood Pressure in Pregnancy, 2000) .

It is expected in normal placental development for the trophoblasts to invade the arterioles of the uterine endometrium for the complete remodelling of maternal arterioles into large blood vessels with low resistance. However, in patients with pre-eclampsia this adaptational response does not occur and thus resulting in insufficient blood supply to the placenta and consequently vasoconstriction (Guyton & Hall, 2006). It is for this reason that preeclampsia is considered to be more than hypertension; but rather a systemic syndrome (National High Blood Pressure Education Program Working Group in High Blood Pressure in Pregnancy, 2000).

Increased maternal arterial stiffness in women destined to develop PE has been related to the 'aberrant maternal physiological and biochemical adaptation to pregnancy that these women demonstrate' (Savvidou, et al., 2011).

Among these are increased maternal endothelial dysfunction resulting from ischemia of the placenta as stated above (Savvidou, et al., 2003), increased levels of asymmetric dimethyl-arginine (ADMA),homocysteine and insulin resistance.

ADMA, an inhibitor of nitric oxide synthase, also causes an increase in the adhesion of monocytes on the vascular lining and consequently arterial stiffness (Savvidou, et al., 2003).

Persons with elevated concentrations of homocysteine are more predisposed to endothelium dysfunction which reduces endothelial relaxation (Jin, et al., 2007). Also, increased insulin resistance decreases the bioavailability of nitric oxide and therefore impairing vasodilation (Steinberg, et al., 1996,Steinberg, et al., 2000,Arcaro, et al., 2002)consequently leading to arterial stiffening,(Wolf, et al., 2002,Dodds, et al., 2008).

‘Changes in arterial stiffness have also been attributed to levels of vasoactive substances such as progesterone, relaxin and volume expansion of pregnancy’ (Khalil, et al., 2009).

2.3 EFFECTS OF ARTERIAL STIFFNESS

Arterial stiffness increases systolic pressure by ‘first, increasing the amplitude of the initial pressure wave generated by ventricular ejection and second, by causing reflected waves from the periphery to return during systole and so augment the initial wave’ (O'Rourke, 1990).

In turn, in stiffer arteries the diastolic pressure is decreased reducing coronary perfusion pressure and also compromising the delivery of oxygen to vital parts of the body. Arterial stiffness has been attributed to be a root cause of left ventricular hypertrophy, left ventricular failure, aneurism formation and rupture amongst others (Koelwyn, et al., 2012).

2.4 COMPLICATIONS OF ARTERIAL STIFFNESS

Aortic stiffness varies throughout the gestation period of a normotensive pregnant individual. It is at its lowest (nadir) in the second trimester and rises in the third trimester (Khalil, et al., 2009). Consequently, as a result of the adaptive changes that take place in a pregnant woman, both central systolic and diastolic blood pressures decrease when compared to non-pregnant controls. However, no significant changes are seen in both carotid- femoral and carotid- radial PWV between these two groups (Macedo, et al., 2008). In PIH, increases in central blood pressures and PWVs in comparison to normotensive controls has been attributed to increased aortic stiffness (Kaihura, et al., 2009) with further increases expected amongst the black population. PWV in women with established PE were 18% higher than the normotensive controls (Kaihura, et al., 2009). This was considered significantly high because aortic PWV, in healthy individuals, increases by~ 6% per decade (Avolio, et al., 1983) . Stiffening has also been seen in other vascular pathways such as the base of the aorta to the popliteal artery (Tihtonen, et al., 2006).

Increased risk of future cardiovascular events has been found in women with a history of PE (Bellamy, et al., 2007).

This has been attributed to the increases in maternal arterial stiffness that these women exhibit (Kaihura, et al., 2009) and consequently increased carotid-femoral PWV (Elvan-Tas¸pinar, et al., 2005).

2.5 BLOOD PRESSURE CHANGES IN PREGNANCY

Blood pressure decreases in normal pregnancy when compared to non-pregnant individuals.

This is due to the remodelling of the arterial system that occurs in normal pregnancy (Guyton & Hall, 2006) as described above. This remodelling however does not occur in PIH and is said to cause increases in arterial stiffness which consequently leads to hypertension.

2.6 PERIPHERAL AND CENTRAL BLOOD PRESSURE

Arterial blood pressure can be measured by methods which record from peripheral sites as done by the routine auscultation method or can be done by measuring from within the large blood vessels as is done in central blood pressure measurements. It has been noted that central blood pressures may not necessarily be the same as peripheral blood pressures but central blood pressure has been described as a better predictor of cardiovascular events (Khalil, et al., 2009).

CHAPTER THREE
METHODS AND MATERIALS
3.1 STUDY SETTING

The study was conducted at the Department of Obstetrics and Gynaecology at the University Teaching Hospital (UTH). Participants were recruited from the antenatal clinic where they attended for the regular routine visits. PWV and related measurements were conducted in a sideroom within the department.

3.2 TARGET POPULATION

The target population included all pregnant women presenting to UTH, Department of Obstetrics and Gynaecology for a routine antenatal visit.

3.3 STUDY POPULATION

The study population 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.

3.4 STUDY DESIGN

This was a cross sectional study.

i. **Inclusion criteria**
   - Pregnant women with consent
   - Age range 18-45 years

ii. **Exclusion criteria**
   - Pregnant women younger than 18 years and older than 45 years
   - Women with chronic hypertension, diabetes mellitus and known cardiovascular pathology.

iii. **Research variables**

The variables used included Carotid-Femoral (C-F) PWV, Carotid-Radial (C-R) PWV, central and peripheral blood pressures.

3.5 SELECTION OF STUDY PARTICIPANTS

The sampling method comprised of the selection of all pregnant women via systematic sampling technique with a sampling interval of 9

3.6 SAMPLE SIZE

At an 80% power with a 1:1 ratio, using a two sample comparison of means at 95% confidence interval and standard error of 0.05, the required number of participants is 14. However, it is recommended by the department of physiological sciences that this number be increased to 30.

3.7 METHODOLOGY

i. 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.

ii. Anthropometric measurements

Body height was measured to the nearest 0.1cm using the Seca Brand 214 Portable Stadiometer (Secagmbh& Co. kg Humburg, German). Participants were asked to remove their foot and head gear with their heels against the back board looking ahead before measurements were taken. Weight was measured to the nearest 0.1kg using the Heine Portable Professional Adult Scale 737 (Secagmbh& 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 either the femoral artery or the radial artery recording sites was measured using a Figure-Finder tape measure.

iii. 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 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); and for the carotid-femoral segment (C-F PWV) palpation was done on the neck for the carotid artery and the femoral artery on the groin.

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 did not move or speak. All measurements were taken by the same two observers for all participants.

3.8 PLAN FOR DATA ANALYSIS AND DOCUMENTATION

i. Analysis

Continuous variables will be summarised using means and standard deviations (or medians and ranges if the variables are not normally distributed). Categorical variables will be summarised using counts and percentages.
The data collected will be entered directly into the data editor of SPSS version 19.0 computer software statistical package.

ii. Documentation

Data will be stored on trusted computers which are password protected. No names will be stored patients will be identified only by unique research laboratory numbers.

3.9 ETHICAL CONSIDERATIONS

Participants were invited to participate in measurements that are non-invasive and provide minimal discomfort. All measurements were undertaken in a clinical research unit which is an environment specifically designed for participants to feel relaxed and comfortable. Any abnormal results found during the study were highlighted and feedback to the patient's consultant obstetrician for action as

appropriate. Participation in this study was voluntary and denial to participate did not have consequences on the treatment of the participant. The participant was free to withdraw from the study at any time. Written consent was obtained.

CHAPTER FOUR
RESULTS
4.1 ANTHROPOMETRIC MEASUREMENTS

A total of 34 women participated in this study. Of these, 14 were normotensive, 12 were newly diagnosed hypertensive and 8 were already diagnosed as pregnancy induced hypertension and were on antihypertensive treatment.

All groups recorded similar age ranges with means of 27, 31 and 29 years for the normotensives, hypertensive participants and hypertensive participants on treatment respectively. The mean gestational age was also similar in all blood pressure groups with normotensives having the widest age range (standard deviation=12). Details of these characteristics are outlined in table1.

Table 1 Baseline characteristics of study groups

	Normotensives (NTN) n=14	Hypertensive (HTN) n=12	Hypertensive on treatment (HTT) n=8	P value
Maternal age (yrs)	27 ± 6	31 ±5	29 ±7	0.136
Gestational age (weeks)	26 ±12	29 ±7	28 ±6	0.901
Weight (kgs)	72 ±15	77 ±15	76 ±13	0.652
Height (cms)	164 ±8	154 ±32	160 ±5	0.599

Values are given as means ± standard deviation. Asymptotic significances displayed across all study groups. The significance level is 0.05. Test used was kruskal-wallis.

4.2 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

	NTN	HTN	P value
bSBP (mmHg)	93 ±9	124 ±18	0.000*
bDBP (mmHg)	59±8	78 ±10	0.000*
bPP (mmHg)	34±6	46±12	0.004*
bMAP (mmHg)	70±8	93±12	0.000*
Carotid – Femoral (C-F) measurements			
cSBP (mmHg)	88 ±10	126±21	0.001*
cDBP (mmHg)	60 ±9	81 ±12	0.001*
cMAP (mmHg)	69 ±8	96 ±14	0.000*
cPP (mmHg)	28 ±9	45 ±12	0.019*
Carotid –Radial (C-R) measurements			
cSBP (mmHg)	86 ±10	119 ±18	0.000*
cDBP (mmHg)	59 ±8	78 ±10	0.000*
cMAP (mmHg)	68 ±7	90 ±13	0.000*
cPP (mmHg)	27 ±11	37 ±15	0.031*

*bSBP=brachial systolic BP, bDBP= brachial diastolic BP, bPP=brachial pulse pressure, bMAP= brachial mean arterial pressure, cSBP=central systolic BP, cDBP= central diastolic BP,cMAP= central mean arterial pressure, cPP= central pulse pressure. Values are given as means ± standard deviation. The significance level is 0.05. Mann-whitney u test was used. * shows significant difference*

Mean central BPs were similar with 88/60 under C-F measurements and 86/59 under C-R measurements amongst the normotensive participants. The hypertensive participants recorded mean central BPs of 126/81 for C-F measurements and 119/78 for C-R measurements which were both higher than those recorded in the normotensives.

Table 3 shows recordings made for augmentation pressures and PWVs.

4.3 PWV MEASUREMENTS

crPWV recorded 9 ±4m/sec for normotensives and 13 ±7m/sec for hypertensive participants (p=0.041). However a cfPWV recording of 8 ± 3m/sec amongst normotensives and 7 ± 2m/sec amongst hypertensive participants did not yield a significant difference (p>0.05).

Table 3 Pulse Wave velocity (PWV), augmentation pressure (AP) and augmentation index (Aix)

	NTN	HTN	P value
Carotid – Femoral (C-F) measurements (n=12) (n=5)			
cfPWV (m/sec)	8 ±3	7 ±2	0.879
AP (mmHg)	4 ±3	10 ±9	0.130
Aix (%)	-1 ±27	-17 ±26	0.574
Carotid –Radial (C-R) measurements (n=14) (n=12)			
crPWV (m/sec)	9 ±4	13 ±7	0.041*
AP (mmHg)	4 ±5	9 ±8	0.046*
Aix (%)	1 ±22	16 ±23	0.031*

*AP= augmentation pressure, Aix= augmentation index, PWV= pulse wave velocity. Values are given as means ± standard deviation. The significance level is 0.05. Mann-whitney u test was used. * shows significant difference.*

4.4 AUGMENTATION PRESSURE

Using the cfPWV measurements, normotensive participants recorded AP of 4 ±3mmHg,and the hypertensive participants, 10 ±9mmHg. With the crPWV measurements, normotensives recorded 4 ±5mmHg and hypertensive participants, 9 ±8mmHg.

4.5 AUGMENTATION INDEX

For Aix, using the cfPWV measurements, normotensive participants recorded -1 ±27% and amongst hypertensive participants, -17 ±26%. With the crPWVmeausrements, normotensive participants recorded 1 ±22% and amongst the hypertensive participants, 16 ±23%.

Significant differences were recorded for the AP and Aix under the C-R measurements (p=0.046,0.031 respectively). However this was not the case for C-F measurements.

4.6 PULSE WAVEFORM

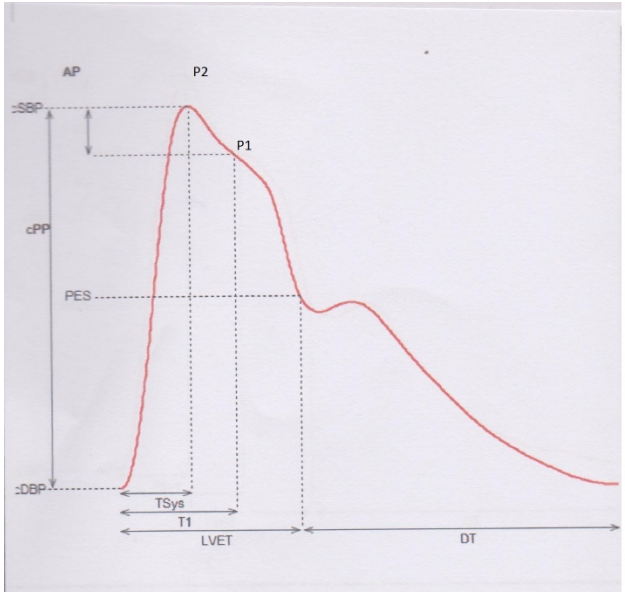

Figure 3 A representative recording of pulse waveform from a normotensive participants; cSBP= central systolic BP,cPP=central pulse pressure, cDBP=central diastolic BP, AP= augmentation pressure, PES= end systolic BP, Tsys=timing of the systolic wave, T1= timing of the reflected wave,LVET= left ventricular ejection time, DT= diastolic time, P1= first systolic peak, P2=second systolic peak

The Tsys period was completed before the T1 period elapsed. Thus consequently P2 preceded P1.

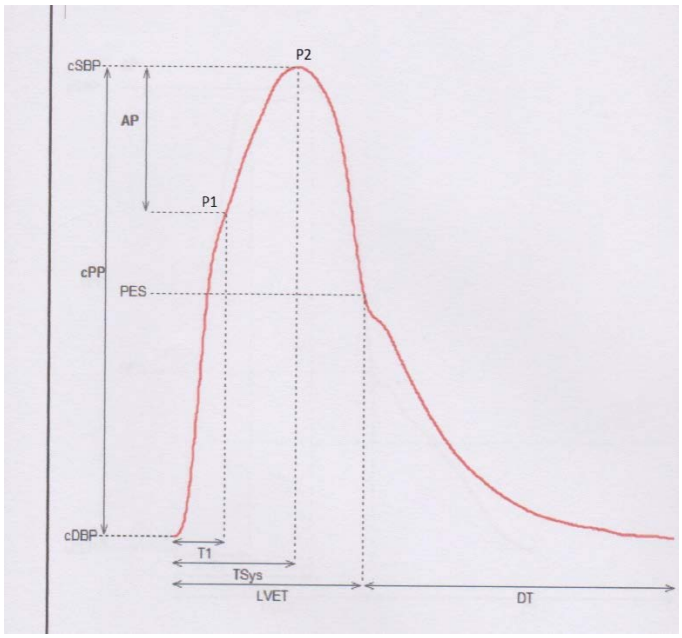

Figure 4 A representative recording of pulse waveform from a hypertensive participants; cSBP= central systolic BP,cPP=central pulse pressure, cDBP=central diastolic BP, AP= augmentation pressure, PES= end systolic BP, Tsys=timing of the systolic wave, T1= timing

of the reflected wave, 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.

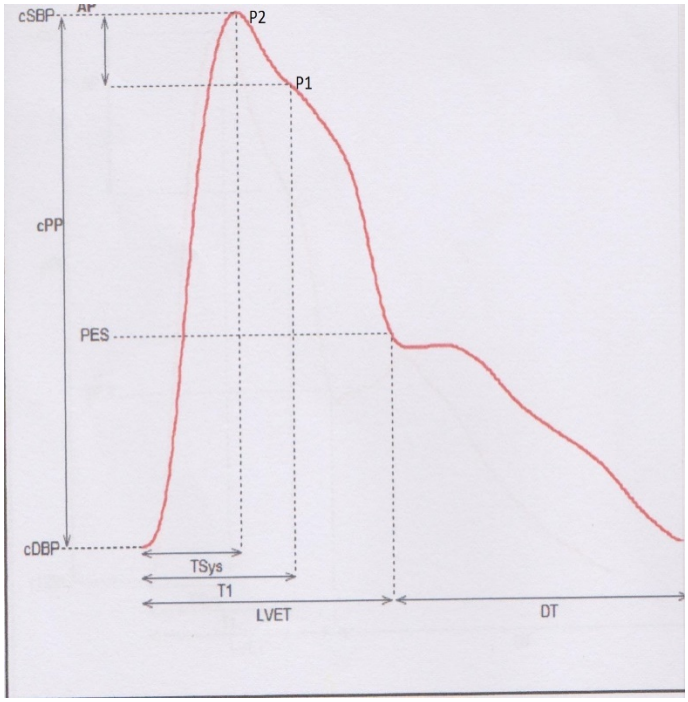

Figure 5 A representative recording of pulse waveform from a hypertensive participants on treatment;cSBP= central systolic BP,cPP=central pulse pressure, cDBP=central diastolic BP, AP= augmentation pressure, PES= end systolic BP, Tsys=timing of the systolic wave, T1= timing of the reflected wave, LVET= left ventricular ejection time, DT= diastolic time,P1= first systolic peak, P2=second systolic peak

The Tsys period was completed before the T1 period elapsed. Thus consequently P2 preceded P1.

Both normotensive and hypertensive participants on treatment showed that Tsys (the timing of the systolic wave) period was completed before theT1 period elapsed (timing of the reflected wave).This translates that the reflected wave arrived in late systole (type C wave). However for hypertensive participantsT1 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 0.01 (n=26).

A moderate positive correlation was seen between central and peripheral systolic pressures and crPWV rho=0.396 and 0.423 respectively at significance of 0.05 level with shared variance of 15.68% and 17.89% respectively.

CHAPTER FIVE
DISCUSSION
5.1 DEMOGRAPHICAL DIFFERENCES

The age groups of all consenting participants showed no statistical significant difference and thus were comparable (p=0.136).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 (Avolio, et al., 1983). 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' (Nichols, et al., 2011). 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 statistically significant differences amongst these categories, participant groups were comparable.

5.2 BLOOD PRESSURE

This study joins many other studies in establishing statistical 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.

5.3 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 (Boutouyrie, et al., 2010).

A statistical significant difference was found in Aix between hypertensive pregnant women and normotensive participants using the crPWV. This suggests that

significant arterial stiffness was exhibited and consequently the reflected wave returned before ventricular ejection in hypertensive participants.

5.4 PULSE WAVE VELOCITY (PWV) MEASUREMENTS

This study has attempted to establish mean PWV values in normotensive and hypertensive pregnant women of African descent. PWV was measured between the carotid radial and carotid femoral arteries. crPWV showed statistical significant difference between these two groups. This suggests that endothelial dysfunction has occurred along the carotid-radial segment which spans the subclavian, brachial, and radial arteries (Mitchell, et al., 2010), 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=0.396, cDBP; rho=0.626, bSBP; rho=0.423, bDBP; rho=0.590) That is, hypertensive participants had a higher PWV than normotensive participants.

However, no statistically significant difference was found in cfPWV. This has been attributed to the unreliability of the recorded results. They were particular difficulties reported in the location of the femoral artery especially during advanced pregnancy (only 5 participants out of 12 had cfPWV readings). This is seen in the outliers recorded from the results which also give a wide standard deviation.

The radial and femoral arteries are different in structure with the radial artery being described as more muscular with less elastic fibres in comparison with the femoral artery. Elastic arteries are made of a large number of collagen and elastic fibers and are able to accommodate more blood for a small rise in pressure than muscular arteries. (Nichols, et al., 2011). Therefore, changes in blood pressure would be easily seen in elastic arteries in comparison to muscular arteries.

cfPWV is considered the gold standard in the measurement of arterial stiffness because of the nature of the arterial system it spans. However, this does not discount the use of crPWV as arterial stiffness is also evident along this arterial system. Also crPWV is easier to measure as no displacement of the radial artery occurs in advanced pregnancies.

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 (Agasti, 2010). This was evidenced by the strong positive correlation seen between crPWV and diastolic blood pressure (rho=0.626).

The waveforms generated were typical to those described in literature (Kaihura, et al., 2009, Khalil, et al., 2009,Savvidou, et al., 2011). A C-type wave was generated in both normotensive and hypertensive participants on treatment.

This wave depicts the return of the reflected wave in late systole after ventricular ejection has ceased, characteristic in young adults (>30 years) (Segers, et al., 2011,Complior analyse operator manual, 2013). Therefore, this study suggests that the use of anti-hypertensive treatment, directly or indirectly, affects the waveforms. Drugs have been said to have little direct effect on arterial stiffness but can reduce wave reflection (O'Rourke, 1990). However, the mechanism of action of these drugs is either indirectly as a sympathetic nervous system inhibitor or calcium blocker (Mustafa, et al., 2012).

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) (Segers, et al., 2011,Complior analyse operator manual, 2013). 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.

5.5 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 (Kaihura, et al., 2009).

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.

Even though all participants were measured in the left lateral position, difficulties were found in the location of the femoral artery and therefore its PWV measurement. This was particular in participants in the third trimester and/or overweight individuals.

As was seen in this study, of the 12 participants investigated, only 5 were measured for carotid-femoral measurements. It was suggested that these difficulties could be attributed to the displacement of the femoral artery with advanced pregnancy. This could have contributed to the lack of significant differences in the cfPWV.

CHAPTER SIX
CONCLUSIONS

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.

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APPENDIX

i. QUESTIONAIRE

GENERAL INFORMATION

1. ID number: ……
2. Age (at last birth day)……. years
3. How long have you been pregnant?.....weeks
4. Marital status single [ ] married [ ] divorced [ ] widowed [ ]
5. Occupation
   ……..
6. Nationality zambian [ ] non zambian [ ]
   a) if non Zambian please state nationality ……

SMOKING

7. Do you currently smoke any tobacco products such as cigarettes, cigars or pipes?
   a) Yes *(IF YES GO TO QUESTION 8)*
   b) No *(IF NO GO TO QUESTION 10)*
8. Do you currently smoke tobacco products daily?
   a) Yes *(IF YES GO TO QUESTION 9)*
   b) No *(IF NO GO TO QUESTION 9)*
9. On average, how many of the following products do you smoke each day/week?

	DAILY	WEEKLY
MANUFACTURED CIGARETTES		
HAND-ROLLED CIGARETTES		
PIPES FULL OF TOBACCO		
CIGARS		
OTHER.....		

10. During the past 30 days, did someone smoke in your home?

a) Yes
b) No

11. For how many days were you exposed to this smoke?.....days

12. **During the past 30 days, did someone smoke in closed areas in your workplace (in the building, in a work area or a specific office)?**

    a. Yes
    b. No
    c. Don't work in a closed area

13. For how many days were you exposed to this smoke?.....days

ALCOHOLIC CONSUMPTION

14. Do you drink alcoholic beverages?
    a) Yes [ ] IF YES GO TO QUESTION 15
    b) no [ ] IF NO GO TO QUESTION 16
15. How often do you consume alcohol?
    a) Everyday
    b) 3-5 times a week
    c) Once a week
    d) Only on weekends
    e) On special occasions

FAMILY MEDICAL HISTORY

16. Is there history of diabetes mellitus in your family? Yes [ ] no [ ] I don't know [ ]
17. Is there history of hypertension in your family? Yes [ ] no [ ] I don't know [ ]
18. Have you ever been told by a doctor that you have diabetes?
    Yes [ ] no [ ]
19. Are you currently taking insulin or pills to control diabetes?
    Yes [ ] no [ ]
    a) If yes please state the
       type…….
20. Are you currently taking medication prescribed by a doctor to lower your blood pressure?
    Yes [ ] no [ ]
    a) If yes please state the
       type…….

PHYSICAL ACTIVITY

21. Does your work involve vigorous- intensity activity that causes large increases in breathing or heart rate like carrying or lifting heavy loads, digging or construction work for at least 10 minutes continuously?
    Yes [ ] no [ ]
22. In a typical week, on how many days do you do vigorous intensity activities as part of your work?
    _____days
23. Does your work involve moderate- intensity activity that causes small increases in breathing or heart rate such as brisk walking or carrying or lifting light loads, for at least 10 minutes continuously?
    Yes [ ] no [ ]

24. In a typical week, on how many days do you do vigorous intensity activities as part of your work?
    _____days
25. Do you walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places?
    Yes [ ] no [ ]

26. In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?
    _____days
27. How much time do you spend walking or cycling for travel on a typical day?
    _____hours _____minutes

ii. IFIPUSHO

IFYAKWISHIBA PALI IMWE

1. ICHISHIBILO:……..
2. Umwaka (ubushibwakulekeleshailyomwafyelwe)…….imyaka
3. Nilisamwalipabukulu?.....imilungu
4. Mulibashimbe [] mwaliupwa [] mwalilekana [] mwalifwilwa []
5. Imilimomubomba……..
6. Chalonshimwafumako Zambian [] non Zambian []
   a) ngatamulibamunocholasoseni……..

MULAPEPA

7. Bushemulapepakofwakangaimishanga, cigars, nangupaipi
   a) ee (kabiyenikwipusho 8)
   b) awe (ngamwakanakabiyenikwipusho 10)
8. Bushemulapepafwakalyonse
   a) ee (kabiyenikuchipusho 9)
   b) awe (ngamwakanakabiyenikuchipusho 9)
9. Nifwakaingamupepachilabushiku/pamulungu?

	Chilabushiku	Pamulungu
Fwakaiyapangwa		
Fwakaiyakupombakuminwe		
Paipiiyaisulanafwaka		
Cigars		
Fimbi…….		

10. Bushe pa mweshiuwa pita, palibauwalepepafwakamunganda mu mwenu?
    a. ee
    b. awe

11. Ninshikushingamwalimupepinabalepepafwaka?.....inshiku
12. Panshinkuumweshiumo, bushekwaliuwalepepaukomwalingakunchitonungukuchikulwamubombela?
    a. ee (kabiyenikuchipusho 13)
    b. awe (ngamwakanakabiyenikuchipusho 14)
    c. nshibombelamunchendeiyaisalwa(ngamwakanakabiyenikuchipusho 14)
13. Ninshikushingamwalimupepinabalepepafwaka?.....inshiku

ABANWA UBWALWA

14. Bushemulanwaubwalwa?
    a) Ee (ngamwasuminakabiyenikulipusho 15)
    b) Awe (ngamwakanakabiyenikulipusho 16)
15. Mikuingamunyaubwalwa
    a) Chilabushiku
    b) Imikuitatunanguisano pa mulungu
    c) Umukuumo mumulungu
    d) Panpelayamulungu
    e) Elyokuliukusefwa

IFISHINKA FYA MALWELE PA LUPWA

16. Bushepalibauwalwalashugamulupwa? Ee [ ] awe [ ] nshaishiba [ ]
17. Bushepalibauwalwalaubulwelebwakubutukaumulopamulupwa? Ee [ ] awe [ ] nshaishiba [ ]
18. Bushebalimwebapoatimwalilwalaubulwelebwashuga? Ee [ ] awe [ ]
19. Bushemulanwaumutiwashuga? Ee [ ] awe [ ]
    a) Ngamulanwaumutiwashugalandenimutinshi?.....
20. Bushemulanwaumutibashingangabamwebauwakubweshaimubutukileyamulopa? Ee [ ] awe [ ]
    a) Ngamulanwalandenimutinshi?.....

IFYAKU CHICHITA

21. Busheimilimoyenu, intuyakakataiingalengaukulapemashikakwatinamusendaifyafina, nangu mule imbaumukandapashitaamaminetiikumi? Ee [ ] awe [ ]
22. Bushemumulungumikuingamubombamoimililoiyakakata?_____inshiku
23. Busheimilimomubombailalengaukutimwalapemashikakwatinamwinyaifipenangumuleendeshasanapamaminetiikumi? Ee [ ] awe [ ]
24. Bushemumulungumikuingamubombamoimilimoiyakakatangaimo pa milimoyenu?_____inshiku
25. Bushemulabofwaichinga pa nshitaukufikapamaminetiikumi, pakuyaukomulefwaya?
    Ee [ ] awe [ ]
26. Bushemumulunguumoninshikushingamwendananguukuninaichingakuyaukomulefwaya pa nshitaaminetiikumi?_____inshiku
27. Busheninshitaingamuposa pa kwendananguukuchofaichingapabushikubumo?_____hawa_____mineti

iii. LABORATORY ENTRY TOOL

1. ID number:.....
2. DATE OF BIRTH:.....
3. STUDY NO:.....
4. VISIT DATE:.....

BLOOD PRESSURES

1. LYING (AFTER 3 MINUTES)

S/N	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)	PULSE
1			
2			
AVERAGE			

2. STANDING (AFTER 1 MINUTE)

S/N	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)	PULSE
1			
2			
AVERAGE			

DISTANCES

MEASUREMENT	**DISTANCE (cm)**	**INITIALS**
RIGHT CAROTID TO RADIAL ARTERY (COMPLIOR)		
RIGHT CAROTID TO FEMORAL ARTERY (COMPLIOR)		

COMPLIOR

CENTRAL sBP | | | |

AORTIC Aix | | | |

	PWV (m/sec)	HEART RATE	TRANSIT TIME	TRANSCRIBED
CAROTID-RADIAL				
CAROTID FEMORAL				

iv. INFORMATION SHEET

My name is Longa Kaluba. I am a master's student in the department of physiological sciences at the University of Zambia, School of Medicine.

The study you are being invited to seeks to investigate how blood flows in pregnant women between 18-45years. We also want to compare whether blood flow is differentbetween those with normal blood pressure to those with high blood pressure. Therefore we will be measuring both women with normal and high blood pressures

The procedure will include getting some general information from you and then applying probes on the neck, arm and leg. The probes may be uncomfortable but will only be applied for a maximum of 10 minutes.

The participant will also be asked to wear a 24hour Diasys Ambulatory Blood Pressure Monitoring system on their non dominant arm which will measure their 24hour blood pressure. Participants will be asked to return it to the laboratory the next day at their own convenience. All measurements will be undertaken in a clinical research unit at the University of Zambia Ridgeway campus (UTH). Any abnormal results found during the study will be highlighted and feedback to the patient's consultant physician for action as appropriate.

The information collected in this study will be stored on trusted computers which are password protected. No names will be stored. Participants will be identified only by unique research laboratory numbers.

Discomfort may be felt once the probes are placed on the neck, arm and leg during the measurement. Also, during the 24hour blood pressure measurement, participants will be asked not to take a bath during the time of investigation.

Participation in this study will be voluntary and denial to participate will have no consequences on the treatment of the participant. The participant will be free to withdraw from the study at any time. Also if participants feel they are not being cared for, they are allowed to withdraw at any time during the procedure.

For more information please feel free to contact the researcher at the following contact detailsLonga Kaluba, Department of physiological Sciences, University of Zambia, School of Medicine.Phone number: 0966/0955 660702

Or

The Chairperson, ERES Converge IRB, 33 Joseph Mwilwa Road, Rhodes Park, Lusaka.

Phone number 0955 155633-4

v. INFORMED CONSENT FORM

The purpose of the study has adequately been explained to me and I understand the aim, benefits, risks and confidentiality of the study. I further understand that; if I agree to take part in this study, I can withdraw at any time without having to give an explanation and that taking part in this study is purely voluntary.

I _____
(Full Names)

Consent to participate in this study

Signed; _____ date; _____
(Participant)

Participant's signature or thumb print

Signed; _____ date; _____
(Witness)

Name of the interviewer; _____

Signed; _____date; _____

PERSON TO CONTACT FOR ANYTHING

Longa Kaluba, University of Zambia, School of Medicine, Department of Physiological Sciences, P.O. Box 50110, Lusaka, Zambia. Mobile Phone; 0966/0955 660702.

OR

The Chairperson, ERES Converge IRB, 33 Joseph Mwilwa Road, Rhodes Park, Lusaka.

Phone number 0955 155633-4

vi. IFILELANDWA PO

Ishinayandi nine Longa Kaluba, ndimwana we sukulumuchiputulwa ca Physiological Sciences pesukululya University ya Zambia, mwisukululya Medicine.

Isambililomwitilwekoyakufwailisha pa lwamulopamulibana mayo balipabukulu,ukufumaabali ne myakaikumina chine konsekonse, ukufikanabaline myakaamakumiyanenayasano (18-45).
Ukukufwailishatulefwayaukwishibaumusangoumulopaubutukilamongabalyaababano bulwelebwamulopawakukubutukisha. Eichotwakulapimabonsebana mayo abo abakwataumulopawakubutukishanaboabashakwata.

Umusangoumoukafumamukusangaamepushoyamoukufumakuliimwe.
Elyonokuyabofyaukuchechentaumukoshi, amaboko, namolu. Ukukuchechenta limo kutikwabaukukanaufwabwino, lelotukala mu chechentafye pa nshitaiinonoukufikapaliamaminetiikumi

Abo bakalapimwabakalafwaikwaukufwalakama shine akapimaumulopapabushikubumo.
Elyoukubokokumbitukalachechentaifyoumulopauleendapanshitaimoine. Aba bakalapimwabakafwaikwaukubwelaubushikubukakonkapopanshitaiyobalefwaya.
Fwonseififikalachitikwa mu chiputulwachaba Clinical research pesukululya University of Zambia Ridgeway Campus (UTH).
Ngachakutitwasangamoifintufimbiifishilipaliukuukufwailishatukebabambibashingan gaabengamwafwalisha

Ukukufwailishakonsetukasangamotukasungilamuma computer ayakwataicakuyacingililanga (password). Ishinalyenutatwakabikepo. Abakala mu chechentabakalaishibilakuli research laboratory number.

Kuli abo bakalachechentwabakatwataishukolyakwebwaifyoumulopawendakumutima.
Elyobakababikaumotusungilainkamashimoishotumonanokusangaifyoabakwataamafy ayamulopawaukubutukishayaba.

Limo tamwakaleufwabwinoilyobakala mu chechenta pa mukoshi, pamaboko, na mu molu. Elyolintubakamupimapalwakubutukakwamulopamukepushiwaukuti, tamufwileukusambapaliubobushiku.

Abo bakabapaliukukusambilabakabafyeabapela.

Elyonangumwakanatakwakabeubwafyabwakumundapailyomulefwaya.

Elyoinshitaiiliyonsekutimwalekangatamulefwayaukukonkanyapo.

Elyongamwamonaukutiabale mu chechentatabaposelekomano, kutimwalekaukukonkanyapo.

Nganamukwataifipushokutimwaishibishabakachechentapeshinapesamba.

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Phone number 0955 155633-4

MALEMBO YAKUSUMINA

Ifilefwaikwamuliukukuchechentanokulondololanabalondola, nokufwaningufwa, nefyoninganonkelamo, elyonamafyaayalimo. Elyotapalinanguumouubengebapaliine. Kabiliningufwafyonse, elyoninsuminaukubulakoulubalipaliukukusambilila. Elyokutinalekapanshitaiiliyonse, ukwabulaukupelaubulondoloshi, Elyoukusangwapaliukukuchechentakuipelafye ne mwine.

Nine_____(amashina yonse)

Ukusuminaukusangwapaliukukusambilila

Ukusaina;_____Ubushiku;_____(abakasangwa po)

Kubakasangwakoukusainananguukubofyaicikumo

Ukusaina;_____Ubushiku;_____(kamboni)

Ishinayakwakepusha;_____

Ukusaina;_____Ubushiku;