ANGLIA RUSKIN UNIVERSITY

EFFECT OF SLOW AND DEEP BREATHING ON CLINICAL BLOOD PRESSURES AND A PILOT STUDY ON ITS EFFECTIVENESS IN PREGNANT WOMEN

NWOBODO NZERIBE, NNENNA HARMONY

A thesis in partial fulfilment of the requirements of Anglia Ruskin University for the degree of MPhil in Medical Technology

This research was carried out In collaboration with Newcastle University, United Kingdom and Enugu State University Teaching Hospital, Parklane, Enugu, Nigeria

Submitted: August 2016
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ANGLIA RUSKIN UNIVERSITY
ABSTRACT

FACULTY OF MEDICAL SCIENCES
MASTERS OF PHILOSOPHY

EFFECT OF SLOW AND DEEP BREATHING ON CLINICAL BLOOD PRESSURES AND A PILOT STUDY ON ITS EFFECTIVENESS IN PREGNANT WOMEN

NWOBODONZERIBE NNENNA HARMONY

August 2016

There is no study investigating the effect of deep breathing on clinical BPs measured simultaneously by manual auscultatory and automatic techniques. This research aimed to provide scientific evidence on the comparison of the effect of deep breathing on manual auscultatory BPs and automatic BPs, and will also preliminarily investigate the effect of deep breathing on pregnant subjects.

The first study involved thirty-nine healthy subjects. The manual systolic and diastolic BPs (SBP and DBP) and MAP were obtained from each subject under resting and deep breathing conditions. During the manual measurement, the oscillometric cuff pressure was simultaneously recorded to determine automated SBP, MAP and DBP, which were cuff pressures corresponding to 50%, 100% and 70% of the waveform envelope, fitted to the oscillometric pulse amplitude. Finally, the effect of deep breathing on both manual and automated BPs were compared.

Experimental results showed that deep breathing significantly (all \( p<0.001 \)) decreased manual SBP, MAP and DBP by 3.5, 3.7 and 3.7 mmHg, respectively, when compared with the resting condition. Automated SBP, MAP and DBP were also decreased significantly (all \( p<0.001 \)) by 2.0, 3.4 and 3.2 mmHg, respectively. In addition, it is observed that 56%, 62% and 67% of subjects showed SBP, MAP and DBP reductions with deep breathing in both manual auscultatory and automatic oscillometric techniques.

The second study involved twenty pregnant subjects. Automated SBP and DBP were measured from each subject at different time points (before, during and after deep breathing). The automated BPs were then compared between the different time points. Experimental results showed that deep breathing decreased automated SBP and DBP significantly \( (p<0.001) \) by 6.4 and 4.8 mmHg. Similarly, automated SBP and DBP measured after deep breathing were also significantly \( (p<0.001) \) decreased by 5.6 and 4.5 mmHg, respectively. Over 70% of the subjects had either SBP or DBP reduction during and after deep breathing.

In conclusion, both manual and automatic BPs were significantly decreased with deep breathing. Over half of the normal healthy subjects achieved significant BP reductions with deep breathing in both manual and automatic techniques. Additionally, it has been demonstrated by our pilot study that deep breathing can be potentially used as a management tool to reduce BPs for some pregnant women.

Keywords: Deep breathing, Pregnancy Induced Hypertension (PIH), Diastolic Blood Pressure (DBP), Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP), Automated, Manual
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<th>Description</th>
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<tbody>
<tr>
<td>ACE</td>
<td>Angiotensin-Converting Enzyme inhibitor</td>
</tr>
<tr>
<td>ACOG</td>
<td>American College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>ADA</td>
<td>American Diabetes Associate</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of Variables</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blocker</td>
</tr>
<tr>
<td>ASA</td>
<td>American and Stroke Association</td>
</tr>
<tr>
<td>ASSHP</td>
<td>Australasian Society for the Study of Hypertension in Pregnancy</td>
</tr>
<tr>
<td>BHS</td>
<td>British Hypertension Society</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium Channel Blocker</td>
</tr>
<tr>
<td>CHS</td>
<td>Canadian Hypertension Society</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic Blood Pressure</td>
</tr>
<tr>
<td>ERS</td>
<td>European Respiratory Society</td>
</tr>
<tr>
<td>ESC</td>
<td>European Society of Cardiology</td>
</tr>
<tr>
<td>ESH</td>
<td>European Society of Hypertension</td>
</tr>
<tr>
<td>ESUT</td>
<td>Enugu State University of Science and Technology</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FFR</td>
<td>Frequency Following Response</td>
</tr>
<tr>
<td>GH</td>
<td>Gestational Hypertension</td>
</tr>
<tr>
<td>HELLP</td>
<td>Haemolysis Elevated Liver and Low Platelets</td>
</tr>
<tr>
<td>Inc</td>
<td>Incorporated</td>
</tr>
<tr>
<td>ISH</td>
<td>International Society of Hypertension</td>
</tr>
<tr>
<td>ISO</td>
<td>International Standard Organization</td>
</tr>
<tr>
<td>JNC</td>
<td>Joint National Committee</td>
</tr>
<tr>
<td>JNCDETH</td>
<td>Joint National Committee on Detection, Evaluation, and Treatment of High blood pressure</td>
</tr>
<tr>
<td>JSH</td>
<td>Japan Society of Hypertension</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean Arterial Pressure</td>
</tr>
<tr>
<td>MATLAB</td>
<td>Matrix Laboratory</td>
</tr>
<tr>
<td>NHBPEP</td>
<td>National High Blood Pressure Education Program</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute of Health Care</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>PE</td>
<td>Preclampsia</td>
</tr>
<tr>
<td>PIH</td>
<td>Pregnancy Induced Hypertension</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic Blood Pressure</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SEM</td>
<td>Standard Error Mean</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Products and Software Solution</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
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<tr>
<td>TETFUND</td>
<td>Tertiary Funding</td>
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CHAPTER 1 Blood Pressure (BP) and its measurement techniques

This chapter gives a general overview of BP and its measurement techniques. The treatment of hypertension is also discussed with emphasis on non-pharmacological treatment using respiratory exercise.

1.1 General overview of BP

Blood pressure (BP) is one of the most regularly recorded clinical parameters in human physiological studies for over 250 years, for both clinical and research purposes (Shapiro, et al., 1996; Pickering, et al., 2005). In 1711, BP was observed by Stephen Hales, a Church of England clergyman, who assumed that blood should be under pressure to circulate. He proved his hypothesis by penetrating a hollow brass glass tube needle into the artery of a horse leg, and observed that there was a regular rise of blood in the hollow brass glass tube. This observation has been recorded in a book titled “Statistical Essays” in 1733 (Wood and Griffith, 1997).

Generally speaking, BP is associated with arterial pressure as it pumps blood from the heart to other parts of the body (Wood and Griffith, 1997; Fahey, et al. 2004; Martini and Nath, 2009). The heart is the major blood pumping organ. It circulates blood to other parts of the body through the arteries and arterioles. During the process, oxygen and food substances are transported to the body, while carbon dioxide and other waste products are excreted out. The whole circulation process relies on blood being under pressure (Fahey, et al. 2004).

As the heart regularly pumps blood out, the muscles in walls of arteries and arterioles contract and expand during blood circulation. When the heart contracts to pump blood to the body, pressure is at its highest point. When the heart relaxes and expands to be filled with blood, pressure is at its lowest point. The highest pressure point of BP is known as the systolic blood pressure (SBP) while the lowest pressure point is known
as the diastolic blood pressure (DBP) (Wood and Griffith, 1997). On the other hand, as the heart beats, BP varies at different sites in the body. It is higher at the aorta and large systemic arteries and relatively lower at the venules and veins (Tortora and Derrickson, 2007; Davies, Blakeley and Kidd, 2011).

BP is normally expressed in millimetres of mercury (mmHg) and recorded as a fraction, having SBP as the numerator and DBP as the denominator. It is generally written as SBP/DBP (Seeley, et al., 1995; Poulter, Thom and Kirby, 2001).

1.2 Classification of BP

BP is classified into low BP, normal BP, pre-high BP and high BP, depending on the readings of SBP and DBP. BP readings vary from person to person, and from time to time. It may also depend on the posture, exercise and stress of an individual. Figure 1.1 shows a BP chart for easy classification of BP. The vertical axis represents the SBP which ranges from 50 to 170 in mmHg while the horizontal axis represents the DBP which ranges from 30 to 100 mmHg. The figure is also indicated by colour to determine normal BP (green), high BP (red), pre-high BP (orange) and low BP (blue) (Petrie, et al., 1986; National High Blood Pressure Education Program, 2004; Blood pressure UK, 2008; Sharman et al., 2016)

a) Normal BP

Normal BP occurs when SBP reading is between the range of 80 to 110 mmHg and DBP is between 60 to 80 mmHg. To keep normal BP, reduction in salt intake, eating of more fruit and vegetables, keeping to alcohol limit and taking of regular exercise are recommended (National High Blood Pressure Education Program, 2004; Blood pressure UK, 2008; Sharman et al., 2016).
b) Low BP

Low BP, also known as hypotension, is diagnosed when BP reading is consistently lower than 80/60 mmHg. Low BP usually occurs as postural hypotension. For instance, when one stands up normally, blood rushes to lower extremities part of the body like the feet and fingers, which, if not controlled, could cause BP to fall, to offset these blood pools. The body normally reacts involuntarily to control it, by alerting the heart to beat faster and the blood vessels to constrict. If the reaction does not happen or occurs too slowly, postural hypotension occurs (Petrie, et al., 1986; Blood pressure UK, 2008).

Postural hypotension is commonly noticeable in people aged above 60 years old, especially in patients with diabetes.

In addition, low BP could occur when the neck BP is not sufficient enough to supply the oxygen and glucose to support the maximal function of the brain. It occurs easily and often in teenage girls, because they commonly have SBP below 100 mmHg (Petrie, et al., 1986; Fahey, Murphy and Hart, 2004; Sharman et al., 2016).
Low BP can be overcome by adding more salt to diet, being well hydrated, standing up gradually, avoiding standing for a long period of time and wearing of support stockings (Fahey, Murphy and Hart, 2004). Arising slowly from sitting position, performing isometric (hand grip) exercise before arising, eating small breakfast, and drinking two large glasses of water early in the morning are also suggested (Kaplan, 2001).

c) High BP

High BP, also known as hypertension, is when BP readings are measured consistently for a number of weeks at 140 mmHg or above for SBP, and 90 mmHg or above for DBP. A single 140/90 mmHg reading at a particular time is not enough to conclude the diagnosis of high BP. More than two extra readings of such BP measurements are needed to be monitored over time. When a pregnant woman develops hypertension, it is known as Pregnancy Induced Hypertension (PIH) (Rolleston and Camb, 2007; Sharman et al., 2016).

BP readings that persist consistently between (120/80) mmHg and (140/90) mmHg is known as Pre-high BP. Readings of 180/90 mmHg or higher indicates a hypertensive crisis (Petrie, et al., 1986; Fahey, Murphy and Hart, 2004; MacGregor and Kaplan, 2006; Sharman et al., 2016). Symptoms like severe headache, fatigue, confusion, problems associated with vision, chest pain, pounding in the chest, neck or ears, breathing difficulty and blood in urine could indicate the presence of extreme high BP. Persistent hypertension could lead to diseases like kidney failure, stroke or dementia, eye problems and heart disease (Rolleston and Camb, 2007).

Hypertension can be treated by drugs like methyldopa, clonidine, labetalol, hydralazine or oxprenolol, nifedipine, atenolol, verapamil, nitroprusside, thiazide, spironolactone etc. It can also be overcome by weight reduction, regular physical exercise, limited alcohol consumption, stopping smoking, low intake of total and saturated fats, low
intake of dietary salts and overall increase of fruits and vegetable intake (Poulter, et al. 2001; Williams, et al., 2004).

1.3 Non-pharmacological treatment of hypertension

Deep breathing has been widely accepted as one of the key factors imposing a physiological change in BP (Zheng et al., 2012). The following sections will give a general overview on breathing and discuss how deep breathing affects BP.

1.3.1 Breathing

Breathing is the mechanism during which air is inhaled into the lungs and then exhaled via the nose or mouth. Two processes involved during breathing are inspiration and expiration. Normal breathing also called apnea is involuntary and rhythmic (Moini, 2012; Martini and Bartholomew, 2007).

a) Inspiration or inhalation

As shown in figure 1.2, inspiration or inhalation involves taking oxygen into the body. During inspiration, intercostal muscles between the ribs contract, and get the ribs raised upward and outward, the ribcage is then expanded. Also, the diaphragm contracts, flattens, pulls down, and causes an increase in thorax volume. This lowers the pressure inside the thorax and gets air sucked into the lungs (Martini and Nath, 2009; Moini, 2012).

b)Expiration or exhalation

Expiration or exhalation takes carbon dioxide out of the body. During exhalation, intercostal muscles relax and lower the ribs downward, causing the diaphragm to relax and move back upwards. This causes a decrease in thorax volume, which as a result, increases the pressure inside the thorax and forces air out of the lungs (Martini and Nath, 2009; Moini, 2012).
1.3.2 Types of breathing

Breathing pattern is characterized by the rate, depth, timing and consistency of breaths during inhalation and exhalation processes. It differs between individuals depending on their health condition. Table 1.1 shows some typical breathing patterns with brief description (Thibodeau, 2010; Hubbard and Falco, 2015).

Table 1.1: Different breathing patterns (Thibodeau, 2010).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eupnea</td>
<td>Normal breathing rate and pattern</td>
<td>Fever, anxiety, exercise, shock</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Increased respiratory rate</td>
<td>Sleep, drugs, metabolic disorder, head injury, stroke</td>
</tr>
<tr>
<td>Bradypnea</td>
<td>Decreased respiratory rate</td>
<td></td>
</tr>
<tr>
<td>Apnea</td>
<td>Absence of breathing</td>
<td>Deceased patient, head injury, stroke</td>
</tr>
<tr>
<td>Hyperpnea</td>
<td>Normal rate, but deep respirations</td>
<td>Emotional stress, diabetic ketoacidosis</td>
</tr>
<tr>
<td>Cheyne-Stokes</td>
<td>Gradual increases and decreases in respirations with periods of apnea</td>
<td>Increasing intracranial pressure, brain stem injury</td>
</tr>
<tr>
<td>Biot's</td>
<td>Rapid, deep respirations (gasps) with short pauses between sets</td>
<td>Spinal meningitis, many CNS causes, head injury</td>
</tr>
<tr>
<td>Kussmaul's</td>
<td>Tachypnea and hyperpnea</td>
<td>Renal failure, metabolic acidosis, diabetic ketoacidosis</td>
</tr>
<tr>
<td>Apneustic</td>
<td>Prolonged inspiratory phase with shortened expiratory phase</td>
<td>Lesion in brain stem</td>
</tr>
</tbody>
</table>
1.3.3 Deep breathing

Deep breathing is performed by narrowing the diaphragm and expanding the abdomen. During the process, air enters via the nose, fills the lungs and then expands the lower belly. It is sometimes called diaphragmatic breathing or belly breathing. Figure 1.3 shows different techniques of deep breathing, which can be performed on lying or sitting down positions. During deep breathing, maximal amount of oxygen is transferred to the blood stream, which triggers relaxation. Deep breathing is applied in order to calm the body down because it strengthens and triggers the parasympathetic system (Fried, 1993; Mason, et al., 2013; Pattanshetty and Thapa, 2015).

Figure 1.3: Different techniques (lying and sitting down) of deep breathing (Adopted from Sisson, 2012; Raisingchildren, 2014).

1.3.4 Steps involved in practice of deep breathing

The steps involved in practicing deep breathing include:

1) Find a calm or quiet place;

2) Lie down in a supine position, keep back and neck straight, pull the abdomen and breathe in through the nose (count 1,2,3,4 as you inhale if possible). Allow the belly
to expand as the air move in. Allow the expansion to continue upwards towards the chest;

3) Exhale slowly without forcing air out from your lungs. Try to exhale for the same duration of inhaling air (count 1, 2, 3, 4);

4) 3 seconds inhale and 3 seconds exhale of deep breathing is recommended at a start. Extend the length of time of inhale and exhale for each breath, up to 5 seconds. This could get into 6 cycles per minute;

5) Finally, repeat the cycle for several minutes.

1.3.5 How deep breathing affects BP

It has been generally accepted that deep breathing reduces BP. The underlying physiological mechanisms of the effect of deep breathing on BP include: (Guyton, 1961; Hubbard and Falco, 2015)

Firstly, deep breathing makes the blood more alkaline. With enough oxygen into the body, it makes the kidney more efficient in removing sodium from the blood, triggering lower BP (Guyton, 1961; Hubbard and Falco, 2015).

Secondly, high BP is associated with blocked nitric oxide embedded in the endothelial cells of the blood vessels. During deep breathing, there is an increase in transmission of nitric oxide. The blood cells utilize the nitric oxide to communicate to the blood vessels to naturally relax during vasodilation. This results in increase of blood flow as well as reduction of BP (Hubbard and Falco, 2015).

Thirdly, any slight deviation in the oxygen content in the brain affects the feeling and behaviour of an individual. During deep breathing, oxygenation allows the body to absorb its full oxygen quota, which relaxes the brain and calms the cardiovascular system, resulting in reduced stress and decreased BP (Guyton, 1961; Hubbard and Falco, 2015).
1.3.6 Device guided breathing

Several devices have been developed to guide inhalation and exhalation rhythm during deep breathing exercise. It has been reported by Rosenthal, et al., (2000, 2001) and Viskoper, et al. (2003) that BPs could be reduced during deep breathing with a guided device. RESPeRATE is the first guided breathing device that has been clinically approved to lower BP (Cernes and Zimlichman, 2015). Recently, the Food and Drug Administration (FDA) has approved breathing device as a treatment for lowering both stress levels and BP (Sharman, et al., 2011; Cernes and Zimlichman, 2015).

1.4 BP measurement and its importance

Hypertension is among the most common chronic medical disorders, which can destroy cardiovascular organs, if ignored. Accurate, routine and reliable BP measurement is therefore essential for medical diagnosis and for monitoring response to therapy (Poulter, Thom and Kirby, 2001). Figure 1.4 shows a BP measurement by a clinician.

![Figure 1.4: BP measurement by a clinician](Farziana, et al., 2009).

Unfortunately, BP measurement error could be generated from the measurements which do not follow the recommended guidelines (Fahey, Murphy and Hart, 2004). The importance of accurate and reliable BP measurement cannot be over emphasized (Mulrow, 2001; MacGregor and Kaplan, 2006).
Firstly, it could systematically prevent BP overestimation, and reduce the number of patients who inappropriately receive unnecessary treatment.

Secondly, it halts BP underestimation that denies access to essential treatment.

Thirdly, it could reduce the incidence of alleviated cardiovascular situations in people with high BP.

Fourthly, routine and accurate BP measurement helps in early prediction, prevention and treatment of high BP related diseases, including heart disease, kidney failure and stroke which have been shown to be global leading factors to death and disability. Accurate, reliable and routine BP measurement could ultimately reduce health cost for the society.


As recommended, the key points to achieve accurate BP measurement include:

1) Caffeine, smoking, and exercise to be avoided before BP measurement;

2) Subjects to be seated calmly for five minutes in a quiet environment before start of BP measurement;
3) Arm position should be placed at heart level with arm or leg uncrossed;

4) Correct cuff and bladder size should be used. A cuff with bladder should encircle at least 80% of the arm, with lower edge to be at least 2cm above elbow joint;

5) Cuff inflation should be at least 30mmHg higher than the point when there is no blood flow. Deflation should be steadily until the appearance of blood flow, at 2 to 3 mmHg per second;

6) If the korotkoff sounds are weak, subjects are recommended to raise the arm, open and close the hand from between five and ten times;

7) If the first two readings are significantly different by more than 5mmHg, averaged value from two or more readings separated by 2 minutes should be used (Pickering, et al., 2005);

8) BP readings should be recorded at the nearest 2 mmHg;

1.5 BP measurement techniques

As shown in figure 1.5, there are two main BP measurement techniques: invasive and non-invasive techniques.

![Diagram of BP measurement techniques](image)

**Figure 1.5: Diagram of BP measurement techniques.**
a) **Invasive technique**

The history of invasive BP measurement technique has been discussed in section 1.1. Although invasive BP measurement in clinical setting has its disadvantages, it is still the most accurate technique as it measures BPs directly in the arteries as shown in figure 1.6. The pressure bag is regulated by the pressure transducer and automatic flushing system and BP waveform is being displayed (Flaherty, Sher, and Caro, 2005). The disadvantages of invasive BP measurement technique include: it could be very painful and could cause blood bleeding from patients; it could lead to body exposure to some infectious diseases; and it requires a skillful and experienced person to operate. However, it has the advantage of displaying beat-by-beat BP waveforms and gives direct and more accurate BP readings especially in people with low BP (Shapiro, et al., 1996; Unit, 2001).

![Invasive BP measurement technique](image)

**Figure 1.6: Invasive BP measurement technique.**

b) **Non-invasive technique**

Non-invasive technique is an indirect way to measure BP. Currently, there are two commonly used non-invasive techniques of measuring BP: manual auscultatory technique and automatic oscillometric technique.
In general, the advantages of non-invasive BP measurement include the fact that they are normally used for routine examination and monitoring. It is not painful to patients. Also, patients are not exposed to diseases and the risk of excessive blood lost. It is affordable and transportable. (Pickering, et al., 2005; Filipovský, et al., 2016).

1.6 Manual auscultatory technique

In 1896, Scipione Riva-Rocci, an Italian physician, developed the manual BP measurement technique using an occlusive cuff in form of air filled bladder. It is today known as sphygmomanometer. Non-invasive manual BP measurement is achieved by wrapping a non-distensible cuff around the arm, which is inflated until the cuff pressure is above the brachial artery pressure to block blood flow. The cuff pressure is then released slowly, to the point when blood flow emerges back in the artery. As deflation continues, blood continues to flow until when there is full blood flow. The pressure at the point when blood first starts to flow back into brachial artery is the maximum arterial pressure, known as SBP. DBP is the minimum arterial pressure at which blood flow is fully restored back to the artery (FitzGerald and Drumm, 1977; Shapiro, et al., 1996; Benmira, et al., 2016).

In 1905, Nicolai Korotkoff, a Russian physician working at Imperial Medical Academy in St. Petersburg, used a stethoscope placed over the brachial artery to detect the sounds of the arterial pulses during the deflation of pressure in the cuff. The first whooshing sound heard is established to be first korotkoff sound which determines SBP. With further cuff pressure deflation, the artery opens and closes, causing more turbulent blood flow and further sounds to be heard. The last sound heard before complete disappearance of the sounds determine DBP. The sound disappears when the artery opens fully to allow smooth blood flow (FitzGerald and Drumm, 1977; Shapiro, et al., 1996; Imai, et al., 1989; Benmira, et al., 2016).
All the general advantages of non-invasive techniques apply to the manual auscultatory techniques. It is the gold standard clinical BP measurement. However, researchers still show dissatisfaction over the detection of Korotkoff sounds (FitzGerald and Drumm, 1977; Shapiro, et al., 1996; Imai, et al., 1989; Benmira, et al., 2016). The main disadvantages of manual technique includes:

1) It cannot be used in a noisy environment;
2) Observations and readings may differ from observers;
3) It does not give accurate results in infants and hypotensive patients;
4) They cannot be performed by unqualified, unskilled and inexperienced operators;
5) Errors could be introduced due to improper cuff size, poor positioning, calibration or maintenance of manometer, body movement of patients and incorrect arm positioning in relation to heart (Imai, et al., 1989; Benmira, et al., 2016).

Nowadays, manual auscultatory technique includes: mercury sphygmomanometer and aneroid sphygmomanometer.

a) Mercury sphygmomanometer

Mercury sphygmomanometer, as shown in figure 1.7, consists of a manometer, an inflatable cuff bladder, a tube for pressure inflation-deflation and a stethoscope. The mercury manometer measures BP by observing height of mercury column on the display. The mercury column is used as simple gravity-based unit, characterized by millimeters of mercury (mmHg), which has become universally accepted units for recording BPs. Mercury sphygmomanometer has achieved the longest use for non-invasive BP measurement. However, the use of mercury sphygmomanometer is being debatable due to toxicity of mercury to the environment (O’Brien et al., 2003; Fahey, Murphy and Hart, 2004; Zheng, et al., 2011). European Standard recommends that mercury sphygmomanometers should display a warning of carefulness and caution
during usage. The International Standard Organization (ISO) instructs that mercury manometer should incorporate a stopping device at the top of the tube to prevent the spillage of liquid mercury. They also recommend that mercury reservoir should be fitted with stopping device to prevent mercury from flowing into the attached tube (Imholz, et al., 1990; Unit, 2001; Benmira, et al., 2016).

The major disadvantages of mercury sphygmomanometer as pointed earlier lies in the usage of mercury. Mercury spillage when inhaled can cause nausea, shortness of breath, pneumonitis and bronchitis. Long term exposure can lead to memory loss, stupor and coma. More seriously, when mercury is converted to methyl-mercury by microorganisms, it becomes dangerous to fetuses and young children. In addition, air leakage, and obstruction in the cuff could also introduce mechanical errors into the device (Unit, 2001; Filipovský, et al., 2016). Therefore, these environment concerns have led to the imposition of bans in some European countries and supply in the UK is now restricted to healthcare use (Fahey, et al. 2004).

Fig 1.7: Mercury Sphygmomanometer (Fahey, et al. 2004).
b) **Aneroid sphygmomanometer**

In comparison with mercury sphygmomanometers, the reading gauges are generally smaller. Aneroid sphygmomanometers has disadvantage of inaccuracy in BP measurement due to mechanical jolts. Another disadvantage is that the device could be damaged without notice (Fahey, Murphy and Hart, 2004).

![Aneroid Sphygmomanometer](image)

Figure 1.8: Aneroid Sphygmomanometer (Fahey, Murphy and Hart, 2004).

1.7 **Automatic oscillometric technique**

Automatic oscillometric technique was originally established by Marey in 1876 (Pickering, et al., 2005). It operates with the principle of amplitude oscillations of pressure in the cuff. During cuff inflation, each heart beat produces an oscillation in blood vessels, which corresponds to the amplitude of the cuff pressure oscillations. With this technique, BPs are determined indirectly via empirical derived algorithms and displayed electronically Figure 1.9 shows the oscillometric waveform extracted from the deflating cuff pressure (bottom trace) and the oscillometric characteristic ratios for SBP, Mean Arterial Pressure (MAP) and DBP determination. MAP is determined at maximum point of the amplitude, SBP and DBP are estimated by the characteristic ratios of 0.5 and 0.7 respectively (Pickering, et al., 2005; Benmira, et al., 2016).
The majority of automated/digital BP devices, as shown in figure 1.10, operate with oscillometric technique. They operate with manual or electronic pump to introduce pressure to the cuff and do not need stethoscope to detect the Korotkoff sounds. (Pickering, et al., 2005).

Today, the uses of automated BP devices are increasing because individuals are being encouraged to buy their own devices for self-monitoring of BP at home and offices. The 24-hour ambulatory BP monitors also operate with the principle of oscillometric technique. Other automatic BP devices include wearable wrist BP device with an electrically driven pump attached to a wrist cuff, and the continuous non-invasive BP
measurement device with a sensor attached to the fingertip that operates with the arterial pulse wave analysis methods (O’Brien, et al., 2005; Pickering, et al., 2005; Gorostidi, et al., 2016; Hamdani, et al., 2016; Isiguzo, et al., 2016).

It has been widely known that readings obtained from clinically validated automated devices are accepted. The advantages of automatic oscillometric technique include:

1) It is easy to use;
2) It has no observer bias;
3) It is mercury free;
4) It can be used in a noisy environment.

The inconsistency of BP measurement by automatic oscillometric device has been reported by Park, Menard and Yuan (2001). The disadvantages are as follows:

1) They are very sensitive to patient movement and the automatic BP calculation algorithm based on characteristics ratio may not work accurately with motion artifact.
2) It may produce inaccurate reading in patients with heart and circulation problems such as arteriosclerosis, arrhythmia, preeclampsia etc.

Before the automated BP devices could be sold in the market, they need pass the requirement of International Standard Organisation (ISO) with clinical trials. Automatic BP device are normally validated under resting condition. However, for clinical research purpose these automatic BP devices are commonly used under non-resting condition. Unfortunately, automatic oscillometric BP devices are not yet validated for BP measurement under non-resting conditions. The readings from these non-resting measurement are therefore questionable and should be carefully interrupted.
CHAPTER 2 Pregnancy Induced Hypertension (PIH) and its management

The chapter gives a general overview of pregnancy induced hypertension (PIH), including its definition, classification, development, symptoms and diagnosis. It also reviews existing strategies on PIH management. Finally, the aim and objectives of this research work, with the organization of this thesis work, are outlined.

2.1 General overview of PIH

Pregnancy is the period a woman carries a fertilized egg inside her uterus until when the baby is born. Pregnancy period (normally 40 weeks) is known as gestation or conception period (Fleischman, Oinuma and Clark, 2010; Medical dictionary, 2011; Venes, 2013). The whole pregnancy period is divided into three trimesters which is made up of three months each. The first trimester is a period in which the embryo develops, the second trimester is a period in which the embryo turns into a foetus, and the third trimester is a period in which the foetus gains weight and gets ready for delivery (Llewellyn-Jones, 1972; Magowan, Owen and Thomson, 2014).

There are many factors affecting pregnancy, including hypertension, diabetes, risk of premature rupture of membrane, preterm labour, infant respiratory distress syndrome, genital track abnormalities, excess amniotic fluid, deficient of amniotic fluid, sexually transmitted diseases, etc. Among them, hypertension is one of the most significant threats for both the life of mother and fetus during pregnancy (Chesley, 1978; Teklu and Gaym, 2006; Amro, et al., 2015). As reported by McGillivray et al., (1980), hypertension is the second leading cause of neonatal and maternal morbidity and mortality (Arulkumaram and Lightstone, 2013).
2.1.1 Definition of PIH and its classification

A generally accepted definition of hypertension during pregnancy is still lacking. It is usually linked to BP increase during gestational period (Kintiraki, et al., 2015), but it should be noted that lots of definitions have been used based on the classification and diagnosis of high BP during pregnancy. Calder (1992) suggested that hypertension during gestational period should be referred to as PIH. Today, PIH appears to be commonly accepted term to describe high BP during pregnancy. Drife and Magowan (2004) stated that PIH is a multisystem disorder and has the possibility of affecting every organ of a pregnant woman, especially the liver, lungs, kidney, brain cardiovascular systems, etc.

The classification of PIH has been a major concern in health care community among individuals and group researchers. There has been some agreement among different researchers over the PIH classification, as shown in table 2.1.

<table>
<thead>
<tr>
<th>S/N</th>
<th>PIH</th>
<th>Its significance</th>
<th>Start period in gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gestational hypertension:</td>
<td>Hypertension without significant proteinuria</td>
<td>After 20 weeks but disappears within 10 days after delivery</td>
</tr>
<tr>
<td>2</td>
<td>Pre-eclampsia:</td>
<td>Hypertension with significant proteinuria</td>
<td>After 20 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Chronic hypertension:</td>
<td>Present at the booking visit and already taking antihypertensive medication</td>
<td>Before 20 weeks</td>
</tr>
<tr>
<td>4</td>
<td>Eclampsia:</td>
<td>Pre-eclampsia with convulsion</td>
<td>Prolonged pre-eclampsia</td>
</tr>
</tbody>
</table>


2.1.2 Development of PIH

The underlying physiological causes of PIH are still debatable. The American College of Obstetricians and Gynaecologists (ACOG) 2002 reported that PIH occurs with high
BP but manifests after twenty weeks of pregnancy (Symonds, Symonds and Arulkumaran, 2013). Contrarily, the Australian Society for the Study of Hypertension in Pregnancy (ASSHP), National High Blood Pressure Education Program (NHBPEP), World Health Organisation (WHO) and Canadian Hypertension Society (CHS) suggest that the diagnosis of hypertension and the presence of protein in urine are the major symptoms of PIH during pregnancy.

The development of PIH is presented in figure 2.1. As shown, preeclampsia starts to develop and can be diagnosed before the fourth week of pregnancy (first trimester). If left untreated, the symptoms (see figure 2.2) will start manifesting from the twentieth week in the second trimester. Untreated preeclampsia leads to eclampsia. When eclampsia sets in, it could lead to early delivery of the baby at the third trimester (Sibai, 1990; Duckitt and Harrington, 2005; Shennan, 2016; Rolleston and Camb, 2007). NICE clinical guideline (2015) states that normal BP should be below 140 mmHg during pregnancy. However, the normal BP values at the three different trimesters of pregnancy have not been specified.

2.1.3 Symptoms and signs of PIH

![Figure 2.1: Development of preeclampsia during pregnancy (Earlybirds, 2015).]
Symptoms and signs of PIH are the subjective and visible evidences or feelings experienced by a pregnant woman at early stage of PIH. It could be noticed by doctors, nurses, family members, neighbours and sometimes friends. Figure 2.2 and table 2.2 show the common symptoms and signs of PIH (Calder, Dunlop and Dunlop, 1992; Villar, et al., 2006; Kenny, et al., 2010; Maputle, Khoza and Lebese, 2015).

Long persistent signs and symptoms of PIH could eventually lead to the followings:

1) Placental abruption: This could cause abnormal and premature separation of placenta from the inner lining of the uterus;

2) Low birth weight babies: This is due to decrease in blood supply to the placenta.

3) Cardiovascular diseases and respiratory distress may occur;

4) HELLP syndrome: HELLP means Hemolysis Elevated Liver enzymes and Low Platelet count. This may occur even before high BP is detected and could be fatal for both mother and baby, resulting in damaged organ;

5) Death: If convolution occurs, it could lead to coma and death of mother and child.

Figure 2.2: Typical signs and symptoms of PIH (Villar, et al., 2006; Benrubi, 2012).
### Table 2.2: Signs and symptoms of PIH

<table>
<thead>
<tr>
<th>Signs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oedema of face, hands and feet</td>
<td>1. Proteinuria</td>
</tr>
<tr>
<td>Sudden weight gain</td>
<td>2. Abdominal pain, lower back pain</td>
</tr>
<tr>
<td>Restlessness, agitation, dizziness and drowsiness</td>
<td>3. Headache, fever</td>
</tr>
<tr>
<td>Headache, fever</td>
<td>4. Blurred vision</td>
</tr>
<tr>
<td>Ringing or buzzing sound in the ear</td>
<td>5. High blood pressure</td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td>6. Inadequate functioning of the liver</td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td>7. Retinal oedema</td>
</tr>
<tr>
<td>Retinal oedema</td>
<td>8. Breathing difficulty</td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td>6. Hypertension</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Ringing or buzzing sound in the ear</td>
<td></td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td></td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td></td>
</tr>
<tr>
<td>Retinal oedema</td>
<td></td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
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<td>Ringing or buzzing sound in the ear</td>
<td></td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td></td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td></td>
</tr>
<tr>
<td>Retinal oedema</td>
<td></td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Ringing or buzzing sound in the ear</td>
<td></td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td></td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td></td>
</tr>
<tr>
<td>Retinal oedema</td>
<td></td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Ringing or buzzing sound in the ear</td>
<td></td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td></td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td></td>
</tr>
<tr>
<td>Retinal oedema</td>
<td></td>
</tr>
<tr>
<td>Breathing difficulty</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Ringing or buzzing sound in the ear</td>
<td></td>
</tr>
<tr>
<td>Low platelet level in blood</td>
<td></td>
</tr>
<tr>
<td>Inadequate functioning of the liver</td>
<td></td>
</tr>
<tr>
<td>Retinal oedema</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Calder, Dunlop and Dunlop, 1992; Villar, et al., 2006; Kenny, et al., 2010; Maputle, Khoza and Lebese, 2015.
2.1.4 Epidemiology of PIH

According to Osungbade and Ige (2011), PIH has affected between 2 to 10 percent of pregnancies globally. WHO has estimated that this health disorder occurs more in developing countries than in developed countries (Omole-Ohonsi, et al., 2008; Kintiraki, et al., 2015). In developed countries such as North America and Europe, the case has been estimated to be between 5 to 7 percent. In African countries such as Nigeria, South Africa, Egypt, Tanzania and Ethiopia, its occurrence varies between 1.8 and 16.7 percent (Mahaba, et al., 2001; Thiam, et al., 2003; Kimbally, et al., 2007; Omole-Ohonsi, et al., 2008; Olopade and Lawoyin, 2008; Osungbade and Ige, 2014; Kintiraki, et al., 2015). To be specific, Anorlu, Iwuala and Odum (2005) found that, one hundred and thirty seven (137) women out of one thousand eight hundred and three (1803) pregnant women were diagnosed of PIH in one tertiary hospital in Lagos State Nigeria, between February 2001 and August 2002. Gurrier, et al., (2013) recorded in Jahun Hospital, Nigeria, that about four hundred and nineteen (419) pregnant women are diagnosed of hypertension between October 2010 to May 2011. Xie, et al., (2013) reported eighteen thousand, one hundred and seventeen (18,117) women with PIH from their study in Saskatchewan hospital, from January, 1980 to December 2005.

2.2 Diagnosis of PIH

When the signs and symptoms of PIH occur, diagnostic tests should be undertaken to confirm the health disorder in pregnant women. Some of these diagnostic tests are direct while the others are indirect. They are summarized in Table 2.3.

2.3 Management of PIH

PIH management involves early education about general lifestyle and nutrition during pregnancy. Education on warning symptoms is also very vital and should be given during antenatal visits. Several international societies including Joint National
Committee (JNC) on Hypertension, American Diabetes Associate (ADA), American Heart Association/American and Stroke Association (AHA/ASA), European Society of Hypertension (ESH), European Society of Cardiology (ESC) and World Health Organisation (WHO) have recommended measures and lifestyles to prevent PIH which include (Craici, Wagner and Garovic, 2008; Facchinetti, et al., 2009): Reduction of salt intake; taking of at least eight glasses of water a day; adequate intake of protein; fruits and vegetables; adequate intake of routine drugs; adequate exercising and rest.

Proper management at early stage could avoid further complications such as convulsions, cerebrovascular haemorrhage, pulmonary oedema, renal failure, abruption placenta, foetal death, leading to a healthy delivery of a child with minimal trauma to the pregnant mother (Evans, 1989; James, et al., 2010).

However, if signs and symptoms of PIH have manifested, Sibia (2003) suggested that its management strategies should depend on the severity, period and nature of the PIH. The other factors to be considered include the foetal gestation age and its status. Consequently, PIH during pregnancy has created a lot of concerns to mothers, families, clinicians, nurses, etc. (Khalil, Jauniaux and Harrington, 2009), and has generated big challenges over PIH management. This eventually affects societal life and will reduce maternal and perinatal morbidity and mortality. No wonder a lot of studies have been reported on how to effectively manage PIH. (Khalil, Jauniaux and Harrington, 2009; Okafor, et al., 2009; Roberge, et al., 2012; Enaruna, Aziken and Cert, 2014). Table 2.4 provides a brief summary of management of PIH.
**Table 2.3: Summary of diagnostic tests of PIH**

<table>
<thead>
<tr>
<th>Direct diagnosis</th>
<th>Indirect diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure measurement</td>
<td>Proteinuria test</td>
</tr>
<tr>
<td>&gt; 140/90 mmHg</td>
<td>&gt; 5g per 24 hrs</td>
</tr>
<tr>
<td>Weight measurement</td>
<td>Chest radiography</td>
</tr>
<tr>
<td>&gt; 3.6kg after 20th week</td>
<td>Presence of pulmonary oedema</td>
</tr>
<tr>
<td>&gt; 140/90 mmHg</td>
<td>Presence of high resistance index/early diastolic notch</td>
</tr>
</tbody>
</table>

Table 2.4: Management of PIH

<table>
<thead>
<tr>
<th>Management</th>
<th>PIH</th>
<th>Gestational hypertension</th>
<th>Preeclampsia</th>
<th>Chronic hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Admit to Hospital</td>
<td>No</td>
<td>Yes, until BP &lt; 150/100</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2. Treat</td>
<td>No</td>
<td>Apply as 1st line oral Labetalol to keep DBP=80-100 &amp; SBP=&lt;150</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3. Measure BP</td>
<td>At least 4 times a week</td>
<td>Once or twice a week</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4. Test of proteinuria</td>
<td>Daily using automated strip reading device or urinary protein: creatinine ratio</td>
<td>Do not repeat quantification of urine protein: creatinine ratio</td>
<td>Daily using automated strip reading device or urinary protein: creatinine ratio</td>
<td>Test and then monitor weekly: Test kidney function, electrolytes, full blood count, transaminases, bilirubin</td>
</tr>
<tr>
<td>5. Blood test</td>
<td>For routine antenatal care: Test kidney function, electrolytes, full blood count, transaminases, bilirubin</td>
<td>If necessary, blood count, transaminases, bilirubin</td>
<td>If necessary, blood count, transaminases, bilirubin</td>
<td>For routine antenatal care: Test kidney function, electrolytes, full blood count, transaminases, bilirubin</td>
</tr>
<tr>
<td>6. Gestational age greater than 37 weeks</td>
<td>Delivery at 37 week if BP &lt; 160/110 without anti hypertensive drug</td>
<td>Delivery at 37 week if BP &lt; 160/110 without anti hypertensive drug</td>
<td>Delivery at 37 week if BP &lt; 160/110 without anti hypertensive drug</td>
<td>Delivery at 37 week if BP &lt; 160/110 without anti hypertensive drug</td>
</tr>
</tbody>
</table>

(Modified from Sibai 2003; Sibai and Stella, 2009; Haines, Macnab and Rajkumar, 2013; Xie, et al., 2013)
2.4 Pharmacological treatment of PIH

The Japanese Society of Hypertension (JSH) and Japanese Society for the study of Hypertension in Pregnancy published a guideline for basic pharmacological treatment of PIH. The antihypertensive drugs that could be taken is summarized in table 2.5. This is in agreement with the guideline of American College of Obstetricians and Gynecologists Committee (2002). These major guidelines (Podymow and August, 2008; 2011, Arulkumaran and Lightstone, 2013; Xie, et al., 2013; Suzuki et al., 2015; Vadhera and Simon, 2015; Pucci, et al., 2015) consider the severity of PIH with intention of lowering its escalation during treatment.

2.5 Non-pharmacological treatment of PIH using respiratory exercise

Until now, existing pharmacological approaches have done well in treating PIH, although some studies have shown concerns of antihypertensive drugs taken during pregnancy, which are outlined in table 2.5. It is shown that, on average, antihypertensive drugs like monodrug therapy with ACE inhibitors could reduce SBP and DBP respectively by 12.5 and 9.5 mmHg, alpha1-blockers by 14.8 and 12.2 mmHg, calcium channel blockers by 15.3 and 10.5 mmHg, and thiazide and loop diuretics could reduce SBP by 15.3 and 15.8 mmHg respectively and DBP by 9.8 and 8.2 mmHg respectively (Wu, et al., 2005).

Notwithstanding, there have been some suggestions for an alternative treatment of hypertension by respiratory exercise (Kim, 1994; Mason, et al., 2013; Pattanshetty and Thapa, 2015; Tomicic, et al., 2015; Hamdani, et al., 2016). Many studies, as seen in table 2.6a, have shown that deep breathing can reduce BP for normal and non-pregnant hypertensive subjects, which was re-grouped in Table 2.6b depending on the BP techniques employed and the type of subjects recruited, indicating the possibility of introducing non-drug treatment of PIH.
<table>
<thead>
<tr>
<th>Benefits</th>
<th>Concerns (possible effect on pregnant mother)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Antihypertensive Drugs</td>
<td></td>
</tr>
<tr>
<td>Methyldopa (preferred)</td>
<td>None</td>
</tr>
<tr>
<td>Clonidine (alternative)</td>
<td>Life-threatening hypertension</td>
</tr>
<tr>
<td>Proven safety and efficacy</td>
<td></td>
</tr>
<tr>
<td>Depression, hepatic disturbances, haemolytic anaemia may not lower BP adequately</td>
<td></td>
</tr>
<tr>
<td>Limited data on foetal safety</td>
<td></td>
</tr>
<tr>
<td>2 Beta blockers</td>
<td></td>
</tr>
<tr>
<td>Labetalol (alpha and beta blocking agent (preferred)</td>
<td>None</td>
</tr>
<tr>
<td>Atenolol (contraindicated)</td>
<td>Hypertension (possible)</td>
</tr>
<tr>
<td>Safety (similar to methyldopa and may be more efficacious than methyldopa)</td>
<td></td>
</tr>
<tr>
<td>No apparent teratogenic effect</td>
<td></td>
</tr>
<tr>
<td>Larger doses can cause neonatal hypoglycaemia</td>
<td></td>
</tr>
<tr>
<td>IUGR (Intra Uterine Growth Restriction)</td>
<td></td>
</tr>
<tr>
<td>3 Calcium Channel Blockers</td>
<td></td>
</tr>
<tr>
<td>Verapamil (alternative)</td>
<td>None</td>
</tr>
<tr>
<td>Efficacy similar to other oral agents</td>
<td>Hypertension (possible)</td>
</tr>
<tr>
<td>Risk of interaction with magnesium (can cause bradycardia)</td>
<td>No apparent teratogenic effect</td>
</tr>
<tr>
<td>4 Direct Vasodilators</td>
<td></td>
</tr>
<tr>
<td>Hydralazine (preferred)</td>
<td>None</td>
</tr>
<tr>
<td>Nitroprusside (alternative)</td>
<td>Hypertension (possible)</td>
</tr>
<tr>
<td>Efficacious intravenous agent. European Society of Hypertension (ESH) no longer recommends it</td>
<td></td>
</tr>
<tr>
<td>Only considered for life-threatening severe hypertension</td>
<td></td>
</tr>
<tr>
<td>Only considered for life-threatening severe hypertension</td>
<td></td>
</tr>
<tr>
<td>Only considered for life-threatening severe hypertension</td>
<td></td>
</tr>
<tr>
<td>5 Diuretics</td>
<td></td>
</tr>
<tr>
<td>Thiazide</td>
<td>None</td>
</tr>
<tr>
<td>Spironolactone (contraindicated)</td>
<td>Hypertension (possible)</td>
</tr>
<tr>
<td>Usefulness in chronic hypertension</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Volume contraction, electrolyte abnormalities – rare with small doses</td>
<td>None</td>
</tr>
<tr>
<td>Possible foetal anti-androgen effects</td>
<td>None</td>
</tr>
<tr>
<td>Maternal polyneuropathy, tachycardia, drug-induced lupus, neonatal lupus, cyanide and thiocyanate toxicity, can cause bradycardia, tachycardia, drug-induced lupus, thrombocytopenia, tachyphylaxis</td>
<td>None</td>
</tr>
</tbody>
</table>

Table 2.5: Antihypertensive drugs on pregnancy.
Table 2.6a: Past studies on effect of deep breathing on blood pressure (2001-2016)

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Study type</th>
<th>No of Subjects (N/H)</th>
<th>BP Decrease (mmHg)</th>
<th>MAP Decrease (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schein et al., (2001)</td>
<td>Randomized control trial</td>
<td>149</td>
<td>M</td>
<td>15.2</td>
</tr>
<tr>
<td>Rosenthal et al., (2001)</td>
<td>Pre-post observational study</td>
<td>13</td>
<td>M</td>
<td>7.2</td>
</tr>
<tr>
<td>Grossman et al., (2001)</td>
<td>Prospective matched case-control</td>
<td>33</td>
<td>A</td>
<td>7.5</td>
</tr>
<tr>
<td>Grossman et al., (2001)</td>
<td>Prospective matched case-control</td>
<td>3</td>
<td>A</td>
<td>2.9</td>
</tr>
<tr>
<td>Jagomagi et al., (2003)</td>
<td>Randomized control trial</td>
<td>13</td>
<td>M</td>
<td>9.1</td>
</tr>
<tr>
<td>Viskoper et al., (2003)</td>
<td>Randomized control trial</td>
<td>17</td>
<td>A</td>
<td>12.9</td>
</tr>
<tr>
<td>Elliot et al., (2004)</td>
<td>Randomized control trial</td>
<td>149</td>
<td>A</td>
<td>7.3</td>
</tr>
<tr>
<td>Mori et al., (2005)</td>
<td>Randomized control trial</td>
<td>4377</td>
<td>3066 (untreated)</td>
<td>30.6</td>
</tr>
<tr>
<td>Elliot and Izzo, (2006)</td>
<td>Case report</td>
<td>1</td>
<td>A</td>
<td>17</td>
</tr>
<tr>
<td>Parati and Carretta, (2007)</td>
<td>Randomized single blind control</td>
<td>30</td>
<td>A</td>
<td>12.2</td>
</tr>
<tr>
<td>Mourya et al., (2009)</td>
<td>Randomized prospective control</td>
<td>60</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td>Surbramanian et al., (2011)</td>
<td>Randomized control trial</td>
<td>8</td>
<td>Not available</td>
<td>-</td>
</tr>
<tr>
<td>Zheng et al., (2012)</td>
<td>Randomized control trial</td>
<td>111</td>
<td>M</td>
<td>4.4</td>
</tr>
<tr>
<td>Ravi et al., (2015)</td>
<td>Case-control study</td>
<td>30</td>
<td>A</td>
<td>Not available</td>
</tr>
<tr>
<td>Mahtani et al., (2016)</td>
<td>Randomized control trial</td>
<td>494</td>
<td>A</td>
<td>2.5</td>
</tr>
<tr>
<td>Wolff et al., (2016)</td>
<td>Randomized control trial</td>
<td>96</td>
<td>Not available</td>
<td>-</td>
</tr>
</tbody>
</table>

Notes: DBP refers to diastolic blood pressure, MAP to mean arterial pressure.
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Type</th>
<th>BP Reduction (mmHg)</th>
<th>SBP</th>
<th>MAP</th>
<th>DBP</th>
<th>Normal (N) or Hypertensive (H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schein et al., (2001)</td>
<td>Manual (M)</td>
<td>-</td>
<td>15.2</td>
<td>10.0</td>
<td>11.7</td>
<td>Hypertensive (H)</td>
</tr>
<tr>
<td>Rosenthal et al., (2001)</td>
<td>Manual (M)</td>
<td>-</td>
<td>7.2</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Augustovski et al., (2004)</td>
<td>Manual (M)</td>
<td>-</td>
<td>10.9</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Meles et al., (2004)</td>
<td>Manual (M)</td>
<td>-</td>
<td>5.5</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Jagomagi et al., (2003)</td>
<td>Manual (M)</td>
<td>-</td>
<td>9.1</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Zheng et al., (2012)</td>
<td>Manual (M)</td>
<td>-</td>
<td>4.4</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Grossman et al., (2001)</td>
<td>Automatic (A)</td>
<td>-</td>
<td>2.9</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Grossman et al., (2004)</td>
<td>Manual (M)</td>
<td>-</td>
<td>7.5</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Viskoper et al., (2003)</td>
<td>Manual (M)</td>
<td>-</td>
<td>17.0</td>
<td>14</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Elliot et al., (2004)</td>
<td>Manual (M)</td>
<td>-</td>
<td>7.3</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Elliot and Izzo, (2006)</td>
<td>Manual (M)</td>
<td>-</td>
<td>11</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Eriksson et al., (2001)</td>
<td>Manual (M)</td>
<td>-</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
<tr>
<td>Piccioni et al., (2003)</td>
<td>Manual (M)</td>
<td>-</td>
<td>6.9</td>
<td>-</td>
<td>-</td>
<td>Normal (N) or Hypertensive (H)</td>
</tr>
</tbody>
</table>

Table 2.6b: Past studies on effect of deep breathing showing BP technique employed and type of subjects recruited.
2.6 Objectives of this research

It has been reported that deep breathing could decrease manual auscultatory BPs on non-pregnant subjects. The automated BP decrease with deep breathing has also been reported with measurements taken from different automatic BP devices. Unfortunately, automatic devices have not been validated for the non-resting conditions, leading to a question on how confidence the results from these studies of investigating the effect of deep breathing using automatic devices could be. Moreover, there are no quantitative clinical data available on the effect of deep breathing on BPs measured by manual and automatic techniques simultaneously. This research aims to provide quantitative clinical data on the magnitude of simultaneous effect of deep breathing on both manual auscultatory and automated BPs.

Nevertheless, deep breathing could be potentially used for PIH management. However, to the best of my knowledge, there is no study providing evidence on PIH management using respiratory exercises. Before deep breathing can be widely adopted for PIH management, more solid scientific evidence is required. As a preliminary study, our investigation will also be performed on normal pregnant women. The outcome of this research could ultimately lead to the development of a device to guide breathing for PIH patients, and be a stepping stone to the final aim of management and treatment of PIH by respiratory exercise.

The main objectives of this study include:

1) To conduct a comprehensive literature review on BP measurements and PIH management including the effect of deep breathing on BPs;

2) To quantify the effect of regular deep breathing on manual auscultatory BP;

3) To quantify the effect of regular deep breathing on automated BP determined from oscillometric waveforms recorded during manual BP measurement, allowing the
comparison of simultaneous effect of regular deep breathing on both manual and automatic technique on normal healthy subjects;

4) To preliminary quantify the effect of deep breathing on normal pregnant women.

To achieve the above objectives, the following will be conducted:

1) **Understand the physiological measurements on normal healthy subjects and pregnant women:** This involves understanding of BP measurement principle and recommended measurement procedure on human subjects.

2) **Digital signal processing using MATLAB:** This will involve the automatic BP determination from the recorded deflating cuff pressure waveform.

3) **Data and statistical analysis:** This will involve the use of Excel to record all the collected data and then transfer it to SPSS Statistics 17 software package (SPSS Inc., USA). SPSS will be used to perform analysis of variance (ANOVA) for the measurement repeatability and to investigate the effect of deep breathing on both manual and automated BPs. Bland-Altman will be used to illustrate the measurement repeatability and difference in BP changes with deep breathing.

4) **Data summary:** This will involve the comparison of BP changes with deep breathing measured by different techniques (manual and automatic) and BP difference between different breathing conditions (normal resting, during and after deep breathing)

### 2.7 Organization of this thesis

**Chapter One** introduces a general overview of BP and its measurement techniques. The treatment of hypertension is also discussed with emphasis on non-pharmacological treatment using respiratory exercise.

**Chapter Two** gives a general overview of pregnancy induced hypertension (PIH), including its definition, classification, development symptoms and diagnosis. It also
reviews existing strategies on PIH management, the aim and objectives of this research work, and ends with the organization of this thesis work.

**Chapter Three** gives the key methodologies for two studies on normal healthy subjects and pregnant women, including the measurement procedure, data collection, and statistical data analysis.

**Chapter Four** summarizes the results of the simultaneous effect of regular deep breathing on manual and automated BPs, and the comparisons between the changes on both manual and automatic BPs. Finally, the effect of deep breathing on automated BP from pregnant women is also reported.

**Chapter five**, is the final chapter. It discusses the conclusion, some challenges faced during the study and recommendations for future work.
CHAPTER 3 Methodology and data analysis

This chapter explains the measurement protocols and data analysis for two experimental studies involved in this research work. Study 1 is for the simultaneous effect of deep breathing on BPs measured by manual and automatic techniques on normal healthy subjects. Study 2 is for the effect of deep breathing on automated BPs using pregnant subjects, aiming to provide evidence on whether deep breathing can be served for non-pharmacological management to PIH.

3.1 Study 1: Simultaneous effect of deep breathing on manual and automated BPs

3.1.1 Subjects
Thirty-nine (39) healthy normal subjects (24 male and 15 female; 18 to 75 years old) without known cardiovascular diseases were recruited to participate in this study. Any subjects with known history of cardiovascular diseases were excluded from the study. The data collection was done by the research team from Newcastle University, London. An ethical permission was received from the Newcastle & North Tyneside Research Ethics Committee. Anonymized data was analyzed. The investigation conformed to the Declaration of Helsinki, and all subjects gave their written informed consent to participate in the study.

3.1.2 Preparation before BP measurement on normal healthy subjects
The manual BP measurements were operated by a trained observer. Before the manual BP measurement, each subject was asked to seat in a chair comfortably with feet placed on the floor. The arm was supported at heart level. Each subject was given a 5 minutes to rest for cardiovascular relaxation. Other preparations include:
1) Each subject fills in and signs a consent form to participate in the study and to confirm that they have no known history of cardiovascular diseases;
2) Measure the arm circumference using a tape to determine the cuff size;

3) A data collection form was designed to record the name, address, age, gender, arm circumference and BPs obtained during manual auscultatory measurement.

3.1.3 Measurement environment

All the measurements in this study were undertaken in a temperature controlled room at 26 ± 1 °C. The window blinds were well covered to block the sunlight and the ceiling lights were switched on. The room was kept tidy and quiet to make subjects feel comfortable during the measurement and to limit disturbances. No distraction was allowed from the operator during the whole measurement.

3.1.4 Measurement protocol and procedure

Figure 3.1 shows the measurement protocol. During manual BP measurement, the oscillometric cuff pressure was recorded from the cuff to a computer to determine automated BPs (SBP, MAP and DBP) while manual BPs (SBP, MAP and DBP) were measured by a trained and experienced observer using manual auscultatory technique. The same observer was used during the whole experiment. This details are given in the schematic diagram of the measurement system, as shown in figure 3.2.

Figure 3.3 shows the BP measurement protocol. For each subject, two BP measurements were performed under resting and deep breathing conditions. To ensure slow and deep breathing pattern was consistent between subjects, a guided respiratory waveform (5 s inhalation and 5 s exhalation) was displayed on a computer screen for each subject to follow. The order of the two measurement conditions was randomized between subjects. They were then repeated three times giving a total of six BP measurements. A time interval of at least 4 minutes was given between repeat sessions, and at least 1 minute between the two BP measurements within a session, allowing the recovery of cardiovascular hemodynamic. The first measurement session was used to
introduce the subjects to the measurement protocol. A total of 156 BP measurements (from 39 subjects x 2 conditions x 2 repeats) were used for further analysis from all the subjects.

![Block diagram of measurement system of study 1.](image1)

**Figure 3.1:** Block diagram of measurement system of study 1.

![Schematic diagram of measurement system of study 1.](image2)

**Figure 3.2:** Schematic diagram of measurement system of study 1. Manual systolic blood pressure (SBP) and diastolic blood pressure (DBP) were obtained through manual auscultatory technique by an observer. The oscillometric cuff pressure waveform was used to estimate automated SBP and DBP.

![BP measurement protocol of study 1.](image3)

**Figure 3.3:** BP measurement protocol of study 1. During deep breathing condition, the subjects performed deep and slow breathing for about 1 min. During this period, the BP measurement was undertaken.
3.1.5 BP Determination

a) Manual auscultatory BP measurement

A clinically validated manual electronic sphygmomanometer [Accoson Greenlight 300; AC Cossor & Son (Surgical) Ltd, Harlow, UK (Graves et al., 2003) was employed as pressure display to conduct all the manual auscultatory BP measurements. Manual auscultatory BP was measured by a trained and experienced operator under standard cuff deflation rate of 2-3mmHg/s. The same operator was used during this study. The manual SBP and DBP were determined from the appearance and disappearance of the korotkoff sounds, respectively. Manual MAP was estimated from the manual DBP plus one third of the absolute difference between SBP and DBP.

b) Automated oscillometric BP measurement

The oscillometric cuff pressure were digitally recorded to a computer for offline oscillometric waveform analysis as the cuff pressure was deflated at 2-3mmHg/s. A fast sampling rate of 2000Hz was used due to the frequency feature of korotkoff sounds. Automated SBP, MAP and DBP were determined from the recorded cuff pressure using an interactive software developed with Matlab 7.1 (MathWorks Inc. Natick, Massachusetts USA). A 6th order polynomial curve was used to fit to the sequence of oscillometric pulse peaks. As shown in figure 3.2, automated SBP, MAP and DBP were determined from the cuff pressure corresponding to 0.5, 1.0 and 0.7 respectively of the modelled envelope, with SBP lay above MAP and DBP lay below MAP.

3.1.6 Data analysis and statistical analysis

Figure 3.4 shows schematic diagram of data analysis procedure for study 1. BP data obtained from both manual auscultatory and automatic oscillometric techniques were compared under resting and deep breathing conditions. The mean and standard deviation (SD) of both manual and automated BPs (SBP, DBP and MAP) across all
subjects were calculated separately for resting and deep breathing conditions using Excel. The Statistical Package for the Social Science (SPSS) Statistics 17 software package (SPSS Inc., USA) was employed to perform Analysis of Variables (ANOVA) for the measurement repeatability and the effect of deep breathing on both manual and automated BPs.

BP changes with deep breathing were calculated for each subject, separately for SBP, MAP and DBP, and for both manual auscultatory and automatic oscillometric techniques. The mean BP change with deep breathing and standard error mean (SEM) of their changes were obtained across all the subjects. P-value was calculated from within-subject paired changes using one way ANOVA with repeated measures, and a p-value below 0.05 was considered statistically significant. Finally, the percentage of subjects with BP reduction in both manual auscultatory and automatic oscillometric techniques were counted.

![Figure 3.4: Schematic diagram of data analysis procedure for study 1.](image-url)
3.2 Study 2: Effect of deep breathing on automatic BP of pregnant women

3.2.1 Subjects

Twenty healthy pregnant women (aged 19 to 55 years old, and gestational age from three to nine months) were recruited to participate in this study. Any subjects with known history of cardiovascular diseases or other pregnancy-related diseases were excluded from the study. A total of twenty subjects were excluded because of the exclusion criteria. An ethical permission was received from the Park Lane Hospital, Enugu State, Nigeria.

3.2.2 Preparation before BP measurement on pregnant subjects

The same preparation as discussed in section 3.1.2 is also applied here.

3.2.3 Measurement room

All the measurements in this study were undertaken by one experienced observer at the antenatal clinic in the Park Lane hospital. The room was kept tidy to make subjects feel comfortable during the measurement. The subjects were required to keep still as not to get distracted during the measurements.

3.2.4 Measurement protocol and procedure

Figure 3.5 shows the block diagram of the measurement system of study 2. As shown, a clinically validated automatic BP device (Motech Truescan model BPU 500) was used to obtain automated BPs from pregnant women at different timings: before, during and after deep breathing.

Figure 3.5: Block diagram of BP measurement system for study 2.
Before each measurement, all residual air in the cuff was pushed out before wrapping it round the arm. The automated BP device was then placed properly on the table.

Figure 3.6 shows the BP measurement protocol of study 2. For each subject, 5 minutes rest was given before first baseline BP measurement. The subject was then asked to start deep breathing at their own comfortable rate. After the fifth cycle of inhalation and exhalation, while the subject continued breathing, the second BP measurement was obtained. After this, 1 minute rest was given before the third measurement. A repeat session was performed for the whole procedure, giving a total of 6 measurements for each subject. A total of 120 BP measurements were obtained for all the 20 subjects.

All the BP data collected from each subject were recorded on the designed data collection form. Other information included are: date and time of measurement, name, address, age, gestational age, arm circumference and other pregnancy information.

![Figure 3.6: Measurement protocol of study 2.](image)

### 3.2.5 Data and statistical analysis

The data analysis for study 2 was performed using Excel and SPSS. All the automated BP values in data collection forms were transferred into excel, where the means and standard deviation (SD) of automated BPs were calculated across all the subjects separately for the three conditions (before, during and after deep breathing). Next, Bland-Altman plots were produced to demonstrate measurement repeatability. SPSS
Statistics 17 software package (SPSS Inc., USA) was used to investigate measurement repeatability and the effect of deep breathing on automated BPs of pregnant women using ANOVA. Post-hoc multiple comparison was then used to study within-subject BP decrease during and after deep breathing in comparison with resting condition (before deep breathing). The BP changes ‘during and after deep breathing’ in comparison with ‘before deep breathing’ were presented in mean difference ± SEM of difference. A p-value below 0.05 was considered statistically significant. Figure 3.7 displays the block diagram of automated BP comparison for the three conditions.

Figure 3.7: Block diagram of automated BP comparison for study 2.
CHAPTER 4  Results
This chapter presents descriptive and analytical results from both studies: the simultaneous effect of deep breathing on manual and automated BP and the effect of deep breathing on automated BP on pregnant women.

4.1 Results from study1:
(Simultaneous effect of deep breathing on manual and automated BPs)

4.1.1 Subject information
Table 4.1 summarizes the detailed subject demographic information, including age, arm circumference, height and weight.

<table>
<thead>
<tr>
<th>Subjects Information</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Subjects</td>
<td>39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of Male</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of Female</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (Years)</td>
<td>18</td>
<td>75</td>
<td>47</td>
<td>40</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152</td>
<td>192</td>
<td>172</td>
<td>28</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50</td>
<td>105</td>
<td>78</td>
<td>39</td>
</tr>
<tr>
<td>Arm circumference (cm)</td>
<td>24</td>
<td>33</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1: Demographic data of the subjects in study 1

4.1.2 Measurement repeatability on manual and automated BP measurements
The repeatability test showed that manual SBP, MAP and DBP were not statistically significant with p-values of 0.48, 0.64 and 0.27 respectively, and also for automated SBP, MAP and DBP with p-values 0.82, 0.51 and 0.34 respectively. The average BP values from the two repeats were then used as reference values for each subject.

4.1.3 Effect of deep breathing on manual and automated BP
Table 4.2 and figure 4.1 give the overall mean and standard deviation (mean ± SD) of BP under resting and deep breathing conditions for both manual auscultatory and automatic oscillometric techniques. BP changes with deep breathing for both manual
and automated BPs in comparison with resting condition are clearly shown. There was no gender difference in BP between male and female subjects (P>0.05).

Table 4.2: Overall mean and SD of BPs under resting and deep breathing conditions. The mean BP difference in comparison with resting condition and standard error mean (SEM) of their differences are also given.

<table>
<thead>
<tr>
<th>BP parameter</th>
<th>Manual BPs (mmHg)</th>
<th>Automatic BPs (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Mean ± SD)</td>
<td>(Mean difference ± SEM)</td>
</tr>
<tr>
<td></td>
<td>(Mean ± SD)</td>
<td>(Mean ± SD)</td>
</tr>
<tr>
<td>SBP</td>
<td>114.1±10.3</td>
<td>110.5±8.6</td>
</tr>
<tr>
<td>MAP</td>
<td>89.0±7.4</td>
<td>85.3±6.4</td>
</tr>
<tr>
<td>DBP</td>
<td>76.4±7.2</td>
<td>72.6±6.1</td>
</tr>
</tbody>
</table>

Figure 4.1: Left: Manual and automated systolic blood pressures (SBPs), mean arterial pressures (MAPs) and diastolic blood pressures (DBPs) measured under both resting and deep breathing conditions. Error bars are from between subject standard deviation (SD). Right: BP decreases with deep breathing using mean BP decrease and standard error mean (SEM) of BP decrease (**) indicates p < 0.001 in comparison with resting condition, from one way ANOVA with repeated measures.)
To be specific, manual SBP, MAP and DBP decreased significantly (all \( p < 0.001 \)) with deep breathing by 3.5 ± 5.9 mmHg (110.5 ± 8.6 vs 114.1 ± 10.3 mmHg), 3.7 ± 3.7 mmHg (85.3 ± 6.4 vs 89.0 ± 7.4 mmHg) and 3.7 ± 3.7 mmHg (72.6 ± 6.1 vs 76.4 ± 7.2 mmHg) respectively. Similarly, automated SBP, MAP and DBP also decreased significantly (all \( p < 0.001 \)) by 2.0 ± 5.2 mmHg (120.3 ± 8.2 vs 122.3 ± 8.9 mmHg), 3.4 ± 4.7 mmHg (85.5 ± 7.1 vs 89.0 ± 8.3 mmHg) and 3.2 ± 3.8 mmHg (62.4 ± 6.0 vs 65.6 ± 7.2 mmHg), respectively.

Figure 4.2 gives their Bland-Altman plots to illustrate the level of BP reduction with deep breathing measured simultaneously by manual and automatic techniques. To visualize the underlying principle of how automated BP decreased with deep breathing in comparison to that under resting condition. Figure 4.3 gives an example of oscillometric waveform under both resting and deep breathing conditions, and shows a clear shift of SBP, MAP and DBP toward lower pressure region when the waveforms was recorded with deep breathing.
Figure 4.2: Bland-Altman plots showing BP changes with deep breathing, separately for manual and automatic techniques. The limits of agreement (mean±2SD) are shown.

Figure 4.3: Example of oscillometric waveforms illustrating decreased automated systolic blood pressure (SBP), mean arterial pressure (MAP) and diastolic blood pressure (DBP) with deep breathing in comparison with resting condition.
4.1.4 Comparison of manual and automated BP decreases with deep breathing

Figure 4.4 shows the manual BP decrease against automatic BP decrease with deep breathing. Figure 4.5 shows their Bland-Altman plots. The results, as shown in the shaded area of Figure 4.4, show that 56%, 62% and 67% of subjects had SBP, MAP and DBP reduction from both manual and automatic techniques.

Figure 4.4: Comparison of manual and automatic BP decreases with deep breathing. 56%, 62% and 67% of subjects had SBP, MAP and DBP reduction in both manual auscultatory and automatic oscillometric techniques.
Figure 4.5: Bland Altman plots of BP changes with deep breathing between manual auscultatory and automatic oscillometric techniques.
4.2 Results from study 2: (Effect of deep breathing on automated BP of pregnant women)

4.2.1 Subject information

Table 4.3 summarizes the detailed subject demographic information including number of times of pregnancy, gestational age, arm circumference and age.

Table 4.3: Demographic data of pregnant women in study 2.

<table>
<thead>
<tr>
<th>Subjects Information</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group of Subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of subjects</td>
<td>20</td>
<td></td>
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<tr>
<td>First pregnancy</td>
<td>10</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy ≥ second time</td>
<td>10</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>9</td>
<td>40</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>19</td>
<td>37</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Arm circumference (cm)</td>
<td>25</td>
<td>35</td>
<td>29</td>
<td>3</td>
</tr>
</tbody>
</table>

4.2.2 Measurement repeatability of automated BP

Table 4.4 represents the mean and SD of the difference between the first and second repeat of BP measurement. For SBP, their differences were (-1.0 ± 12.8, -1.4 ± 9.5 and -1.3 ± 7.4) mmHg, respectively for the three different measurement points. The corresponding DBP differences were (-1.2 ± 10.9, 0.8 ± 6.7 and -1.1 ± 5.4) mmHg, respectively. There was no significant difference between the repeats (all p > 0.05).

MAP was not considered in study 2 data analysis because the device only provided SBP and DBP values. Figure 4.6 shows the level of agreement between first and second repeat by Bland-Altman plots.

Table 4.4: Mean and standard deviation (SD) of blood pressure (BP) measurement repeatability.

<table>
<thead>
<tr>
<th>Mean and standard deviation (Mean ± SD) of automatic BP differences between repeatability (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1st measurement – repeat)</td>
</tr>
<tr>
<td>Before deep breathing</td>
</tr>
<tr>
<td><strong>SBP</strong></td>
</tr>
<tr>
<td><strong>DBP</strong></td>
</tr>
</tbody>
</table>
Figure 4.6: Bland-Altman plots showing the measurement repeatability between the first and second repeat measurements. The limits of agreement (mean difference ± 2SD) are given.
Comparison of automatic BP measured before, during and after deep breathing

Table 4.5 shows the mean ± SD of automated SBP and DBP across all subjects with the measurement taken before, during and after deep breathing. It shows that SBP decreased significantly by 6.4 ± 11.3 mmHg (103.2 ± 15.7 vs 109.6 ± 15.4 mmHg) during deep breathing and by 5.6 ± 9.6 mmHg (104.0 ± 14.2 vs 109.6 ± 15.4 mmHg) after deep breathing when compared with before deep breathing respectively. Similarly, DBP reduced significantly by 4.9 ± 6.8 mmHg (60.6 ± 9.1 vs 65.4 ± 10.9 mmHg) during deep breathing and 4.5 ± 8.4 mmHg (60.9 ± 9.8 vs 65.4 ± 10.9 mmHg) after deep breathing respectively, when compared with before deep breathing.

Figure 4.7 shows the comparison of automated SBP and DBP measured before, during and after deep breathing. Both SBP and DBP decreased significantly during deep breathing with p=0.001 when compared with before deep breathing. Automated SBP and DBP decreased significantly after deep breathing with p values of 0.003 and 0.001 respectively. There was no significant difference (p > 0.05) for both SBP and DBP between during and after deep breathing.

Table 4.5: Mean and standard deviation (SD) of automated SBP and DBP measured before, during and after deep breathing. Their decreases during and after deep breathing are presented in mean changes and standard error mean (SEM) of changes.

<table>
<thead>
<tr>
<th>BP parameter</th>
<th>Before deep breathing</th>
<th>During deep breathing</th>
<th>After deep breathing</th>
<th>BP decrease with deep breathing (Mean difference ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>During</td>
</tr>
<tr>
<td><strong>SBP</strong></td>
<td>109.6 ± 15.4</td>
<td>103.2 ± 15.7</td>
<td>104.0 ± 14.2</td>
<td>6.4 ± 2.5</td>
</tr>
<tr>
<td><strong>DBP</strong></td>
<td>65.4 ± 10.9</td>
<td>60.6 ± 9.1</td>
<td>60.9 ± 9.8</td>
<td>4.9 ± 1.5</td>
</tr>
</tbody>
</table>
4.2.4 Individual BP changes before, during and after deep breathing

Figure 4.8 shows the individual SBP changes before, during and after deep breathing. Each line represents each subject and BP changes. It is observed that 75% of the subjects had SBP reduction during deep breathing and 70% of subjects after deep breathing. Similarly, Figure 4.9 shows the individual DBP changes before, during and after deep breathing. It is observed that 75% of the subjects had DBP reduction during deep breathing and the same percentage of subjects had DBP reduction after deep breathing.
Figure 4.8: Individual automated systolic blood pressure (SBP) values measured before, during and after deep breathing in pregnant women.
Figure 4.9: Individual automated diastolic blood pressure (DBP) measured before, during and after deep breathing in pregnant women.
CHAPTER 5 Discussion, conclusion and future work

The chapter gives the conclusion, and discusses some challenges faced during the study and recommendations for future work.

5.1 Discussion

This research work included two sub-studies. The first study quantitatively confirmed that both manual and automated BP decreased significantly with deep breathing when compared with resting condition. The second study, as a pilot study, demonstrated that deep breathing could be potentially used to reduce BP for some pregnant women.

5.1.1 Discussion on study 1:
(Simultaneous effect of deep breathing on manual and automated BPs)

This study quantitatively demonstrated that both manual and automated BPs decreased significantly with deep breathing when compared to resting condition. In terms of the changes on manual BP, this is in agreement with previous studies that manual SBP and DBP reduced with consistent practical period of slow and regular deep breathing (Rosenthal, et al., 2000; Schein, et al., 2001; Rosenthal, et al., 2001; Jagomagi, et al., 2003; Augustovski, et al., 2004; Zheng, Giovannini and Murray, 2012). Similarly, the automated SBP and DBP decrease with deep breathing also agreed with published studies with measurements taken from different automatic BP devices (Ravi, Narasimhaswamy and Anand, 2000; Grossman, et al., 2001; Viskoper, et al., 2003; Elliott, et al., 2004; Elliott and Izzo, 2006; Parati and Carretta, 2007).

Unfortunately, there is no quantitative scientific data available on simultaneous comparison of the effect of deep breathing on both manual and automated BPs. Our research work achieved this.

Furthermore, current automatic BP devices are not validated for non-resting conditions, making results from past studies (See table 2.6a) questionable. Our research work was conducted based on the analysis of digitally recorded oscillometric cuff pressure...
waveform to determine automated BPs, alleviating the potential uncertainty of the results from these un-validated automatic BP devices for non-resting conditions.

In this research, a decrease in manual auscultatory BPs with deep breathing has been confirmed with a shift of peak of automatic oscillimetric waveform envelope to lower BP region (Figure 4.3). BP decreases observed in manual auscultatory technique were moderately correlated with decreases of automated BPs determined from automatic oscillometric technique, indicating true physiological effect during deep breathing.

Regarding the underlying mechanisms for the effect of deep breathing on BP, it could include:

1) It has been attributed to reflexes from mechanoreceptors in the lungs. When the lungs expand during deep breathing, these receptors initiate the Hering-Breuer Reflex (HBR), and reduces respiratory rate which eventually leads to autonomic cardiovascular inhibition and reduces BP (Eckberg and Sleight, 1992; Jerath, et al., 2006; Hubbard, and Falco, 2015; Adhana, et al., 2016; Onen, et al., 2016).

2) Deep and slow breathing decreases peripheral resistance and increases blood flow in blood capillaries, which regulates heart rate, and reduces BP (Soyik, 2000; Hubbard, and Falco, 2015; Sharma and Gupta, 2016).

3) Deep breathing triggers the body to absorb its full oxygen quota, exhaling out carbon-dioxide which lowers heartbeat and stabilizes BP (Selvamurthy, et al., 1983; Suckling, et al., 2016; Hubbard, and Falco, 2015).

4) Nitric oxide is utilized by the endothelium cells (cells that line the blood vessels) to communicate to muscles around them to slow down and relax during vasodilation. During deep breathing, the steadiness of nitric oxide is stimulated, allowing the natural relaxation of the blood vessels, thus lowering BP (Guyton, 1961; Baylis, Mitruka, and

5.1.2 Discussion on study 2  
(Effect of deep breathing on automated BP of pregnant women)

Although the past studies have suggested that pharmacological management of PIH has no known effect on the foetus, it have been reported that women with PIH always stand the risk of cardiovascular complication either in the short or long run of their lives (Schachter, 2002; Podymow and August, 2008; Khali, et al., 2009; Magee, et al., 2014). There is need to explore an alternative management strategy. Past studies have shown that BPs from hypertensive patients could be reduced with deep breathing for a short period of time (Schein, et al., 2001; Rosenthal, et al., 2001; Grossmann, et al., 2001; Viskoper, et al., 2003; Meles, et al., 2004; Elliot, et al., 2004, Augustovski, et al., 2004; Mori, et al., 2005; Elliot and Izzo, 2006; Parati and Carretta, 2007; Mourya, et al., 2009; Surbramanian, et al., 2011; Mahti, et al., 2016; Drodz, et al., 2016; Wolff et al., 2016).

However, there is no study investigating the practice of respiratory exercise for controlling of PIH. Results from this study showed that deep breathing had a positive reduction effect on SBP and DBP on normotensive pregnant women, providing the scientific evidence that deep breathing can be served as a potential substitute to pharmacological management of PIH.

5.2 Limitations and challenges

There are several limitations in this research work, which should be addressed:

1) The relatively small number of subjects were involved. This is because the project was conducted and investigated within a short-term period;

2) Some subjects did not follow deep breathing procedure exactly as required. The use of guided device should be a better solution.

3) The effect of slow paced breathing on the foetus has not considered, and
4) Finally, the effect of different gestational age on BP changes with deep breathing has not been investigated.

5.3 Recommendations for future study

In order for the technique of deep breathing to be adopted in clinical and community settings to reduce BP, some recommendations of future work could include:

1) Inclusion of large group of normal pregnant women, as well as PIH patients;
2) Compare the effect of different breathing patterns on BP reduction and select a breathing pattern that can quickly and reliably reduce BP;
3) Investigate the long-term effect of deep breathing on BP;
4) Investigate the difference of BP reduction with deep breathing between male and female subjects.
5) Investigate which BP (SBP, MAP or DBP) is most vital to be reduced for PIH patients.
6) Investigate the effect of gestational age on BP reduction with deep breathing;
7) Investigate the potential effect of slow paced breathing on the fetus;
8) Develop a deep breathing guided device and test its effectiveness;
9) Compare non-pharmacological management with drug treatment;
10) Consider the possibility of deriving respiratory rates from BP measurement.

5.4 Conclusions

In summary, the following could be concluded from the research work:

1) Both manual and automatic BP decreases with deep breathing were statistically significant. Over half of the subjects achieved significant BP reduction with deep breathing in both manual and automatic techniques.
2) Deep breathing can be used to help some pregnant women (over 70% in this study) to reduce BP.
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