HIGH BLOOD PRESSURE - THE SILENT KILLER ON THE PROWL: COMBATING THE ALBATROSS

By

PROF. BASDEN JONES C. ONWUBERE

PRESENTATION OUTLINE

DEDICATION

This lecture is dedicated to the following that have made immense impact in my life as an individual from birth.

- The Almighty God
- My mother – Christiana Rosetta
- My wife – Akwaugo Nkechi
- My daughter – Ezinne Uchechi
- The one billion people worldwide living with the burden of high blood pressure

PREAMBLE

Mr. Vice Chancellor, I most sincerely thank you and the entire University administration for the opportunity to give this 73rd Inaugural Lecture of our great Institution. I also thank the current and the immediate past administrations for the re-awakening of academic and research activities in our University. This is reflected in the increasing number of professorial chairs in the entire University. Records show that this Inaugural lecture series became more regular from 2007. Professor Chinedu Nebo and Professor Batho Okolo are highly commended for this.

Going through records, it does appear that this lecture is the first inaugural lecture from my Department of Medicine. I give God the glory and wish my department, easily the most organized in the University, best of academic progress. I do sincerely hope this lecture would open up the flood gate for more lectures from the department, the College of Medicine, and the entire University academic community.

My previous intention had been to give this lecture in 2011 to mark my 35th year of graduating from this Citadel of Learning but this was cancelled by the University for official but unforeseen circumstances. A re-schedule for June 2012 also did not come to be for some other reasons.

I thank God for this historic event taking place today, and for putting me at the centre of it. It is obviously divine plan to place me as the **73**rd Inaugural Lecturer as the figures '7' and '3' are biblically and culturally significant. This year also marks my **37**th year of graduation!

An inaugural lecture is expected to be on a subject that the lecturer has, indeed, spent a significant part of his academic life participating actively in research and made a reasonable number of publications and general contributions. In my own case, this topic incidentally is not only of public interest but is, in fact, a condition that is expected to be 'silently' affecting approximately a third of the entire audience here today. Over half of those aged 60 years and above are ordinarily afflicted. This is, indeed, a subject I have been rather passionate about and have spent a significant part of my life in its management, control, prevention and rendering administrative service to concerned Organizations. The good news about this 'silent killer' is that if detected early and effectively controlled, morbidity (indisposition) and death could be prevented. In other words, it is reversible and its consequences avertable only if detected early before permanent pathophysiological processes take place.

INTRODUCTION

Blood Pressure

Blood pressure is the force that needs to be maintained to enable blood circulate to all parts of the human body. Blood is the medium by which nutrients and oxygen are sent to all parts of the body. The pressure is generated mostly by the pump action of the heart, a vital organ about the size of the clenched fist of a person. Since the blood flow needs to be maintained without any interruptions, the force is maintained during the relaxation phase of the heart by the elastic recoil of the major arteries thereby providing a continuous flow and supply of vital nutrients to all tissues of the body.

Blood pressure is recorded in two parts: **systolic** (the upper figure)– during the contractile phase of the heart, and diastolic (the lower figure)– during the relaxation stage. Blood pressure is said to be **high** when it exceeds an accepted normal level. **High blood pressure** is also termed **hypertension**, a less descriptive term that appears to be more popularly used. Both terms would be used inter-changeably in this text even though the later gives an impression of a terrible disease entity that sometimes frightens the sufferer. Normal blood pressure at rest is within the range of 100-140mmHg systolic (top reading) and 60-90mmHg diastolic (bottom reading). High blood pressure is said to be present if it is persistently at or above **140/90 mmHg**[1].

High blood pressure is diagnosed on the basis of persistently raised blood pressure levels. This usually requires three separate measurements at one-monthly intervals using the instrument

called **sphygmomanometer**. Initial assessment of a hypertensive individual should include a complete history and physical examination. With the availability of 24-hour ambulatory blood pressure monitors and home blood pressure self-recording machines, the importance of not wrongly diagnosing those who have what is termed 'white coat' hypertension has led to a change in protocols[1]. 'White coat' hypertension arises when fright and apprehension or both affect the blood pressure reading during a visit to a healthcare facility where the personnel traditionally wear white garments.

When an individual's blood pressure is persistently high, it not only puts a strain on the heart but also damages the walls of the arteries, making them stiffer and more prone to clogging and haemorrhage (bleeding). This causes problems in the organs they supply and leads to potentially fatal conditions and incapacitating disorders, such as coronary heart disease and stroke.

Normal levels evolve from scientific evidence. Internationally, the **World Health Organization** (WHO) and the **International Society of Hypertension** (ISH) [2, 3] determine this level. These International bodies regulate the diagnosis and control of hypertension and other disease conditions globally. Regional and national organizations are usually given the responsibility of determining appropriate cut off points and guidelines bearing in mind the regional and national peculiarities and characteristics of the concerned population. It is now agreed that both systolic and diastolic pressures should be addressed in any determined cut-off point. Some of these regional organizations are: The American Society of Hypertension (ASH), the European Society of Hypertension (ESH), the International Forum for control and prevention of Hypertension in Africa (IFHA) and others. The national organizations include the Nigerian Hypertension Society (NHS), the South African Hypertension Society (SAHS), among others[1].

Blood pressure is classified by the WHO/ISH[2, 3] and the various regional and national organizations then adapt to suit their peculiarities based on available scientific evidence. The simplest and one of the latest is that of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) in its 7th Report (JNC7)[4] reproduced below:

Classification (JNC7)[4]

	Systolic pressure (mmHg)	**Diastolic pressure (mmHg)**
Normal	90–119	60–79
Prehypertension	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥160	≥100
Isolated systolic hypertension	≥140	<90

The various hypertension organizations periodically produce evidence-based 'guidelines' for the management of hypertension to guide health-care personnel. These guidelines are not necessarily strict rules but provide evidence-provided recommendations to guide healthcare providers.

High blood pressure is a main factor responsible for premature death in the world and, therefore constitutes the major global burden of disease. It is a key risk factor for stroke, myocardial infarction (heart attacks), heart failure, aneurysms of the arteries (e.g. aortic aneurysm), and peripheral arterial disease. It is a significant cause of chronic kidney disease. Life expectancy of an individual could be considerably lowered even by moderate elevation of (arterial) blood pressure. It has become a major global health concern[5].

The Silent Killer

Uncomplicated high blood pressure is largely without symptoms. Most symptoms are usually those associated with the complications when they occur. This situation has given rise to the name 'Silent-Killer' frequently given to High Blood Pressure and making it a key priority for prevention, detection and control, and one of the most important challenges facing public health today globally. Sufferers who are 'lucky' to have symptoms could have headache, dizziness, tinnitus (ringing sensation in the ears), blurring of vision, palpitations, or symptoms of the specific complications. These individuals are deemed 'lucky' in the sense that they would have compelling need to see health care personnel that would check their blood pressures and possibly detect a significant rise for early intervention, unlike their asymptomatic counterparts.

HISTORICAL PERSPECTIVES

Hypertension was recognized by the early Chinese in the period 2600BC who palpated (felt) the peripheral pulses to determine the 'pressure' in the vessels and treated hard-to-palpate vessels by bleeding and leeches[6]. High blood pressure was then called "hard pulse disease".

William Harvey (1578–1657), an English Physician is given the first position in the modern history of hypertension even though Dr Amatus had earlier given an insight into blood circulation. Harvey in his book, "*De motu cordis*" described completely and in detail the systemic circulation and properties of blood being pumped to the body by the heart[7]. This was not an easy task as expressed by Harvey himself thus: *"...I found the task so truly arduous... that I was almost tempted to think... that the movement of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place by reason of the rapidity of the movement...*"[8, 9].

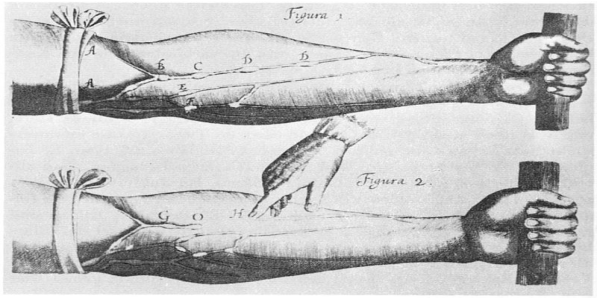

Image of veins from Harvey's *Exercitati Anatomica de Motu Cordis et Sanguinis in Animalibus*

In 1733, Stephen Hales (1677 – 1761), an English clergyman and philanthropist first published **measurement of blood pressure**. He also made significant contributions to a range of scientific fields including botany, pneumatic chemistry and physiology and invented several devices, including a ventilator, a pneumatic trough and a surgical forceps for the removal of bladder stones[7,8, 10].

Descriptions of hypertension as a disease came, among others, from **Thomas Young** in **1808** and **Richard Bright** in **1836**[7].

Frederick Akbar Mahomed (1849–1884), an internationally known British Physician from Brighton, England was the first to report in **1874** a case of elevated blood pressure without evidence of renal disease[11].

A major revolution occurred in **1896** with the invention of sphygmomanometer by **Scipione Riva-Rocci**, an Italian Internist and Paediatrician. This enabled blood pressures to be measured and monitored in the clinics and wards[12].

In **1905**, **Nikolai Korotkoff** improved the technique by describing the Korotkoff sounds that are heard when the artery is auscultated with a stethoscope while the sphygmomanometer cuff is deflated[8].

In **1925**, **Otto Frank**, a German-born doctor and physiologist described the concept of essential hypertension ('hypertonie essential'). This is a common type of hypertension with no discernible cause[13].

In 1928, the term malignant hypertension was coined by physicians from the **Mayo Clinic** to describe a syndrome of very high blood pressure, severe retinopathy and adequate kidney function which usually resulted in death within a year from strokes, heart failure or kidney failure[14].

In **1931**, **John Hay**, Professor of Medicine at Liverpool University who contributed immensely to the knowledge of hypertension, wrote that *"there is some truth in the saying that the greatest*

danger to a man with a high blood pressure lies in its discovery, because then some fool is certain to try and reduce it"[15].

In 1937, **Paul Dudley White**, prominent US Cardiologist reputed for cardiovascular care of many US Presidents, in his book titled "Heart Disease" suggested that *"hypertension may be an important compensatory mechanism which should not be tampered with, even were it certain that we could control it"*[16].

Franklin Delano Roosevelt, the 32nd President of the USA was a prominent person in history known to have severe hypertension. On the afternoon of April 12, **1945** Roosevelt said, "I have a terrific pain in the back of my head." He then slumped forward in his chair, unconscious, and was carried into his bedroom. He died at 3.35 pm same day[17].

In **1949**, **Charles Friedberg** in his classic textbook "Diseases of the Heart"[18,] stated that "*people with 'mild benign' hypertension* ... [defined as blood pressures up to levels of 210/100 mm Hg] ... *need not be treated*"[19]. This corroborated with White's earlier view in 1937 that raised blood pressure needed not be treated[16].

In the **1950's** and after, substantial evidence from landmark actuarial and longitudinal studies like the Framingham studies became available[20,21]. The effect of cardiovascular risk factors (e.g., smoking, obesity, inactivity, diabetes mellitus, etc) in determining the management and outcome of hypertension became widely known. Risk factor identification then became part of routine assessment of the hypertensive subject. Risk factors also came to be recognized as important issues in determining the blood pressure level to initiate drug therapy and in fact the type of medication to be used. Life style modification also became a recommended management strategy for all hypertensive subjects with identified modifiable cardiovascular risks. The recommended cut-off for hypertension has also been lowered in the past fourteen years from 160/95 mm Hg to 140/90 mm Hg based on research-based evidence[1].

Management of high blood pressure in history

In ancient times, "hard pulse disease" was treated by blood-letting by the Chinese and use of leeches by the Greek and Indians[2]. This was advocated by The Yellow Emperor of China, Cornelius Celsus, Galen, and Hipocrates[2].

During the 19th and 20th centuries, effective pharmacological treatment modalities for high blood pressure were yet unavailable, three treatment modalities with significant side-effects were used: strict sodium restriction[3], sympathectomy (surgical ablation of parts of the sympathetic nervous system), and pyrogen therapy (injection of substances that caused a fever, indirectly reducing blood pressure)[22] All through the middle part of the 20th century, the treatment of hypertension was often ineffective. Even Roosevelt, reported to have BP levels greater than

250/150 mm Hg, was only treated with phenobarbital, a low-sodium diet, and rest at the time of his signing the Yalta treaty[17].

After the second world war, **hexamethonium, hydralazine** and **reserpine** (derived from the medicinal plant Rauwolfia serpentina) became available.

It was not until **1957** and **1958** that a major advance occurred with the development of the first thiazide diuretic, **Chlorothiazide** from the antibiotic sulfanilamide[23, 24]. A randomized controlled trial sponsored by the Veterans Administration in subjects with high blood pressure (diastolic BP 90–114 mm Hg) using hydrochlorothiazide, reserpine, and hydralazine versus placebo showed overwhelming benefit in reducing cardiovascular morbidity and mortality in the treated group[25]. The study continued in people with lower blood pressures and showed that treatment even in people with mild hypertension more than halved the risk of cardiovascular death[26].

Beta blockers were developed in the early **1960s** through the pioneering work of Scottish Physician and Pharmacologist, **James W Black** for which he received the 1976 Lasker Award and in 1988 the Nobel Prize in Physiology or Medicine[22].

Calcium channel blockers were the next to be discovered when Verapamil, initially thought to be a beta blocker and used for angina treatment was found to lower blood pressure significantly[16]. This was later found to be effective in Blacks even as monotherapy[27].

Angiotensin converting enzyme (ACE) inhibitors the next group were developed through rational drug design with Captopril becoming available in **1977**[28] and other ACEIs later coming up and confirmed efficacious[22, 29].

More recently **alpha adrenergic blockers** (AABs), **angiotensin receptor blockers** (ARBs) and **renin inhibitors** have also been introduced as antihypertensive agents.[30 - 32].

Table 1 shows dates of discovery of antihypertensive drugs or drug classes[33].

Table 1: Dates of Discovery of Antihypertensive Drugs or Drug Classes

Year(s)	Antihypertensive Agent(s)	Year(s)	Antihypertensive Agent(s)
1900	Sodium thiocyanate	1970s	α2 agonists (eg, clonidine)
1931	Reserpine	1973	β-Receptor blockers
1947 – 1950	Ganglion blockers	1975	α1 receptor blockers
1950s	Hydralazine	1977	ACE inhibitors
1950s	Guanethidine	1977	Calcium channel blockers

1957	Spironolactone	1993	Angio. II receptor blockers
1958	Thiazide-like diuretics	2000	Renin inhibitors
1960	Methyldopa		

ACE indicates angiotensin-converting enzyme. Data derived from Freis[33]

Lifestyle and high blood pressure in history

About **2600 BC** Huang Ti Nei Ching Su Wein made the earliest recorded comment on lifestyle when he wrote: "… therefore if large amounts of salt are taken, the pulse will stiffen or harden" [2], as translated by Wan Ping in **AD 762**.

In **1904**, two French medical students, Ambard and Beaujard[34], were the first to promote the concept that the cause of hypertension was salt in the diet, and they claimed some success in reducing blood pressure by restricting salt. They had incriminated chloride rather than sodium – a proposition later supported by Kotchen and Boegehold [35, 36].

In **1948**, Kempner[37] renewed interest in salt restriction with his introduction of the rice-fruit diet, which contained 150 mg of sodium per day. Pickering[38], in **1968**, condemned this, describing it thus: *"It is insipid, unappetizing and monotonous and demands great care in its preparation, for if the salt rises above 250 mg/d, the effect in most instances is lost."*

In the past quarter of a century several controlled, clinical trials have documented the benefits of reduction of salt intake, other nutritional interventions, stress reduction, weight loss, and other lifestyle modifications on the prevention and treatment of hypertension[39 – 46].

Table 2: Examples of Non-Pharmacologic Trials for the Prevention or Treatment of Hypertension

STUDY	YEAR	OUTCOME
Dietary Intervention Study for Hypertension (DISH)[39]	1985	Weight loss and salt restriction more than doubled success in withdrawal of drug therapy in patients with mild hypertension
Trial of Antihypertensive Intervention Management (TAIM)[40]	1991	In the short term, drugs outperformed diet and weight loss in the treatment of mild hypertension
Trials of Hypertension Prevention (TOHP):	1992	In the short term, weight reduction and, to a lesser extent sodium reduction lowered blood pressure in persons with

Phase I[41]		high normal blood pressures; blood pressure was not reduced by either stress management or nutritional supplements
Trial of Stress Reduction[42]	1995	In the short term, transcendental meditation lowered blood pressure in older blacks with mild hypertension
Dietary Approaches to Stopping Hypertension (DASH)[43]	1997	A diet rich in fruits, vegetables, and low-fat dairy products substantially reduced blood pressure in adults with high normal blood pressures or mild hypertension
Trial of Non-pharmacologic Interventions in the Elderly (TONE)[44]	1998	Weight loss and reduced sodium intake each safely lowered blood pressure in older persons with hypertension
Trials of Hypertension Prevention (TOHP): Phase II[45]	2001	Clinically significant long-term reductions of blood pressure were achieved with modest reductions of weight loss
PREMIER Trial[46]	2003	Individuals with above-normal blood pressure, including stage 1 hypertension, can make multiple lifestyle changes that lower blood pressure and reduce cardiovascular disease risk.

Sub-Saharan Africa

About a century ago, hypertension was known to have low incidence in most parts of Sub-Saharan Africa (SSA).

In **1929,** Donnison [47]in an article published in the Lancet wrote: "Over two years at a native hospital in the South of Kavirondo in Kenya, during which period approximately 1800 patients were admitted, no case of raised blood pressure was encountered, although abnormally low blood pressure was not uncommonly encountered. On no occasion was a diagnosis of arteriosclerosis or chronic interstitial nephritis made". He further observed similar BP patterns in Europeans and Blacks until the age of 40 years after which BP rose in the African and not in the European.[48]. The situation changed after decades with HBP noted from epidemiological studies to be a significant cardiovascular burden and increase of BP patterns noted with age[49, 50]. Of note was the observed lower BP levels in rural than in urban dwellers. The prevalence of hypertension (BP≥160/95 mm Hg) in rural studies undertaken in the 1970s, 1980s, and 1990s has generally been low: 4.1% in Ghana,[51] 5.9% in Nigeria,[52] 7% in Lesotho,[53]and 9.4% in the rural Zulu.[54].

More recent data, such as those from Tanzania, Ghana, Nigeria, Egypt and South Africa, suggest that hypertension prevalence (using a partition value of 140/90 mm Hg) is on the rise in Africa and commonly exceeds 20%–25% in rural areas and is over 30% in urban and semi-urban areas[55 - 60]. The changing pattern has been attributed to increasing urban – rural population drift and rapid urbanization as well as current preference for western-oriented lifestyle[55]. The rising prevalence of diabetes mellitus has also been shown to be highly contributory[48].

To address the rising burden of high blood pressure in SSA, the International Forum for Hypertension prevention and control in Africa (IFHA) was formed in Brussels, Belgium, in **2003** with Nigeria playing a notable role. This resulted in the publication of the first guidelines for the management of hypertension in SSA in **2003**[61].

Nigeria in history

A recent meta-analysis of hypertension in Nigeria[62] revealed that probably, the first report of hypertension study in Nigeria was in **1953** by Callander[63].

In **1955** and **1956**, hypertension was reported as a cause of heart disease by Nwokolo et al[64] and Beet et al[65] respectively.

In **1960,** the first recorded large scale epidemiological study was reported by Abraham et al[66]. Following this, Akinkugbe, generally regarded as the top-most opinion leader on hypertension in Nigeria, published extensively in the 1960s and 1970s[67-76] working with collaborators. Among other findings, they documented that casual systolic and diastolic pressures did not significantly differ from those in Black populations in the Caribbean, but systolic and diastolic values were marginally higher in African Americans than in West Indian or West African Blacks.

Between **1961 and 1981**, there were 36 recorded studies in Nigeria published by various researchers[62]. It is clear from the studies that age was the main determinant of presence of high blood pressure and there was significant increase in the observed prevalence from the first study by Abrahams et al[66] in **1961** to the study by Ladipo in **1981**[77]. Increasing awareness in the populace might contribute significantly to the noted progressive prevalence rate increase over the years of study.

There was also an increasing trend in the prevalence rate of high blood pressure in Nigeria. Pooled prevalence rate of 8.9% was estimated from community-based study available from **1970 to1979**. From **1990 to 1999**, the pooled prevalence of hypertension was 15.0%; with a significant increase to 22.5% from **2000 to 2009**[62]. More recent studies even show higher rates. Onwubere et al[59] in 2011 in a study carried out in rural Ezeagu Community, Enugu State found a prevalence rate of 46.4% in a population aged 40 – 70 years. Ulasi et al[60] in a market survey in Enugu in 2011 had a rate of 42%.

An extensive literature search by Ogah et al[62] documented 43 studies on prevalent rates of hypertension in Nigeria between **1960 and 2012**. Six of these studies were carried out in Enugu State.

There are probably hundreds of publications on hypertension in Nigeria published in local journals that cannot be retrieved online.

The **Nigerian Hypertension Society** was inaugurated on April 27, **1993** at the first scientific meeting held in Lagos with the following objectives:

- To provide knowledge of the prevalence, causes, prevention and treatment of hypertension and its complications.
- To bring together all medical doctors, health professionals and scientists in Nigeria interested in the study and/or control of hypertension.
- To increase the awareness of the disease in the community.
- To establish contact and exchange information with similar organizations in other parts of the world.

The Society is affiliated to the World Hypertension League (WHL) and the International Society of Hypertension (ISH).

The following Presidents have served the Society since inauguration:

1993 –1997 - Emeritus Professor O.O.Akinkugbe

1997 – 2001 - Professor A.F.B.Mabadeje

2001 – 2005 - Professor B.J.C.Onwubere

2005 – 2010 – Professor A.O. Isah

2010 – till date – Professor A Arije

The NHS has published two guidelines for the management of Hypertension: first in **1996** and the second in **2005**[78].

PATHOPHYSIOLOGICAL CONSIDERATIONS

The pathophysiology of hypertension is of prime research interest. Hypertension is classified as 'Essential' or Secondary. Essential hypertension where no medical cause is known constitutes 90 – 95 % of all cases of hypertension[79, 80]. Secondary hypertension (5 – 10%) is a situation where the cause of hypertension is known and usually from kidney, endocrine and vascular diseases.

The pathogenesis of essential hypertension is not only very complex but also involves multiple factors which include genetic predisposition, excessive salt intake, and adrenergic tone. Multiple factors that modulate the blood pressure (BP) to ensure adequate tissue perfusion include humoral mediators, vascular reactivity, circulating blood volume, vascular calibre, blood viscosity, cardiac output, blood vessel elasticity, and neural stimulation. A possible pathogenesis of essential hypertension has been proposed in which multiple factors, including genetic predisposition, excess dietary salt intake, and adrenergic tone, may interact to produce hypertension. Although genetic factors appear to contribute to essential hypertension, the exact mechanism is yet to be fully established[81, 82].

The heritability of hypertension (genetic hypertension) is typically estimated from family and twin studies to be in the range of 30–70%, with multiple contributory genes and gene–gene interactions[83 - 85].

Page, in **1949,** had introduced the concept of a "mosaic theory" to explain the aetiology of hypertension. By this he meant that "… most of the known and probably many unknown control factors could be accommodated as long as they were in equilibrium, maintain blood pressure and tissue perfusion at relative constancy, but still adapting to tissue needs." Essential hypertension was designated a disease of control or regulation, and no constant dominant cause could be expected except in the secondary hypertensions."[86, 87].

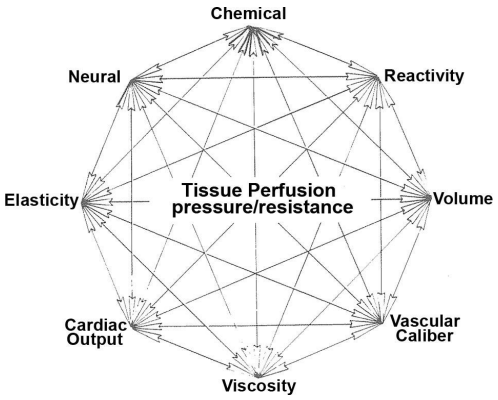

Figure 1: Page's Mosaic theory of hypertension [86]

Guyton in **1967** described a "hierarchy of pressure control systems" that provided both short-term damping and long-term control of arterial pressure[88]. This was followed in **1972** by Brunner et al[89] who emphasized that hypertension was not a single disease but a heterogeneous group of disorders with discrete aetiologies. They observed that over 30% of hypertensive subjects had low renin while 20% had high renin.

Blood pressure is determined by cardiac output and peripheral resistance. Most patients with essential hypertension have a normal cardiac output but a raised peripheral resistance. Peripheral resistance is determined not by large arteries or the capillaries but by small arterioles, the walls of which contain smooth muscle cells[82].

Certain mechanisms have been proposed to account for the increase in peripheral resistance in hypertension. Greatest evidence implicates either disturbances in renal salt and water handling, especially abnormalities in the intra-renal renin-angiotensin system [90] as well as abnormalities of the sympathetic nervous system.[91]. Additionally, it is strongly believed that endothelial dysfunction and vascular inflammation may also contribute to increased peripheral resistance and vascular damage in hypertension.[92, 93].

Pathological consequences (Complications)

I. The Cardiovascular System

• Sustained increased vascular resistance leads to left ventricular hypertrophy (LVH). A concomitant ischaemic heart disease would make this worse. LVH is an independent risk factor of cardiovascular disease and leads to relative myocardial ischaemia from reduced supply of blood from the coronary arteries. In addition to angina pectoris, dysrhythmias (abnormalities with heart rhythm are common in this situation. Diastolic dysfunction, atrial fibrillation and significant ventricular extrasystoles are fairly common. Eventually, left ventricular failure may ensue, consequently leading to congestive heart failure[1, 94 - 97].

• Hypertension enhances coronary atheroma predisposing the individual to myocardial infarction. Heart disease is in fact, the commonest cause of death in hypertensive subjects[94, 95, 98 - 100].

• Atherogenesis in the arteries predisposes to dissecting aneurysm of the aorta, peripheral artery disease, and increased stroke incidence.

Cardiovascular complications are the greatest cause of hospital admissions for hypertensive subjects in Nigeria[101 - 105].

II. Cerebrovascular disease

• The prevalence of both major and minor stroke is higher in individuals with Charcot-Bouchard aneurysms. Hypertensive subjects have greater predisposition to sub-arachnoid haemorrhage if they have Berry aneurysms on the circle of Willis.

• It is recognized that hypertension is the most prevalent risk factor for stroke. Transient ischaemic attacks occur several-fold more in hypertensive subjects than in normotensive persons[106 -108].

III. The Kidneys

• Hypertensive nephro-sclerosis is the major lesion in the kidneys and affects the afferent arteries more than the others. This leads to progressive reduction in renal function.

• Arteriolar fibrinoid necrosis is found in most individuals with malignant and accelerated hypertension.

• Large renal artery branches are prone to atheromatous degeneration causing renal ischaemia.

• Significant renal ischaemia especially at the juxtaglomerular apparatus stimulates the Renin-angiotensin system and further increases the blood pressure[109, 110].

IV. The Eyes

• Atheromatous involvement of the retinal arteries leads to retinal artery thrombosis. The affected individual presents with partial or total field defect (blindness).

• As mentioned earlier, fibrinoid necrosis of the retinal arterioles causes haemorrhages and exudates.

• Papilloedema is the extreme form of hypertensive retinopathy[111].

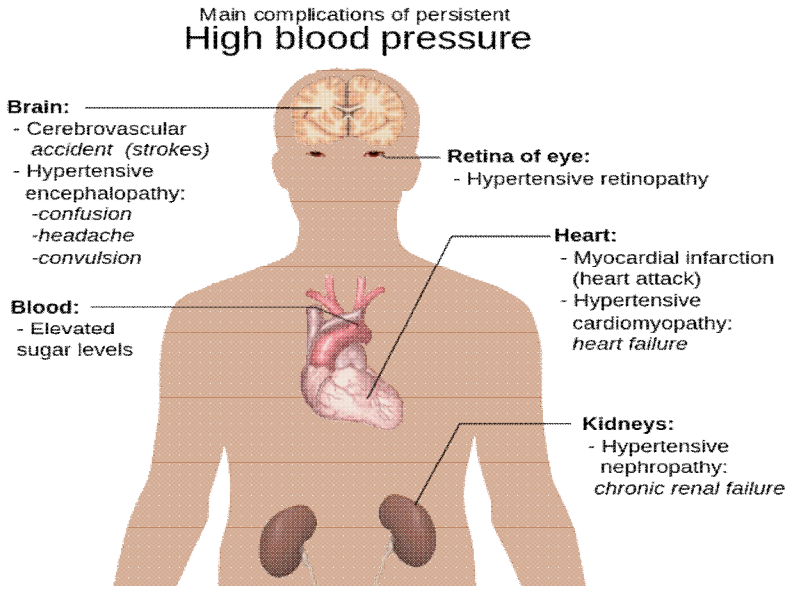

Figure 2: Target organ involvement in hypertension (Source: Hypertension Wikipedia: the free encyclopedia. Retrieved 25 Feb 2013)

A GLOBAL BURDEN – THE KILLER INDEED

High blood pressure constitutes an important public health burden globally[112]. Various observational data attributed BP elevation with systolic values above 115mmHg to be responsible for a total of 7.6 million deaths (13.5% of total global mortality) and 92 million (6% of total) of the sum of deaths and disability adjusted life years (DALYs). It is disturbing that 80% of worldwide cardiovascular-related deaths occur in low-to-middle income countries, and, in comparison with high-income countries, these deaths (and events such as stroke and acute myocardial infarction) occur at a younger age, exerting a profound impact on the family unit and the workforce. It is predicted that non-communicable forms of cardiovascular diseases will become the leading cause of death and disability globally, by 2020[5, 113 - 117].

The prevalence rates of hypertension vary around world-wide with the lowest prevalence in rural India (3.4% in men and 6.8% in women) and the highest prevalence in Poland (68.9% in men and 72.5% in women). The overall prevalence of raised blood pressure in adults aged 25 years and over was around 40% in 2008. Even though the proportion of the world's population with high blood pressure, or uncontrolled hypertension, fell modestly between 1980 and 2008, because of population growth and ageing, the number of people with uncontrolled hypertension rose from 600 million in 1980 to nearly 1 billion in 2008[118].

There is, therefore clear evidence that **global prevalence of hypertension has been increasing**. In 2000, **972** million people had hypertension with a prevalence rate of 26.4%, **333** million in economically developed countries and **639** million in economically developing countries. It is

projected that by 2025 a total of 1.54 billion people accounting for 30% of the World population would be hypertensive with 75% of these from the developing countries and regions[5, 112, 118].

Regarding attributable deaths, the leading behavioural and physiological risk factors globally are raised blood pressure (to which 13.5% of global deaths are attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%) and being overweight or obese (5%)[119].

Evidence shows that raised blood pressure causes 51% of stroke deaths and 45% of coronary heart disease deaths[119]. It is worthy to observe that mean blood pressure has decreased dramatically in nearly all high-income countries. A recent worldwide study from 199 countries and territories involving 5.4 million participants showed that on average, global population SBP decreased slightly since 1980, but trends varied significantly across regions and countries. SBP is currently highest in low-income and middle-income countries. The mean age-standardized male systolic blood pressure (SBP) in the United States decreased from 131 mm Hg (95% uncertainty interval 127–135) in 1980 to 123 mm Hg (120–127) in 2008, while mean age-standardized female SBP decreased from 125 mm Hg (121–130) to 118 mm Hg (115–122) mm Hg[120]. On the other hand, mean blood pressure has been stable or increasing in most African countries. Currently, mean blood pressure remains very high in many African and only few European countries[120 - 122].

According to the 2012 World Health Organization Health statistics for 2012 for Nigeria, the mean SBP was 132 mm Hg in 1980; fell to 128 mm Hg in 1990; and rose steadily to 132 mm Hg in 2008 for Men. For Nigerian women it rose steadily from 129 mm Hg in 1980 to 133 mm Hg in 2008[122].

The silent killer is, indeed, on the prowl!

Ironically, this scourge targets economically weakened and unwary populations that are of course ill-prepared to combat it.

COMBATING THE ALBATROSS

Available data show that lowering blood pressure in people with hypertension is associated with a reduction in cardiovascular disease risk. A large-scale meta-analysis of observational, prospective studies[123] among hypertensive patients aged 40-69 years showed that a 20 mmHg lower SBP is associated with:

■ Less than half the risk of dying from a stroke, and

■ Half the risk of dying from coronary heart disease.

The decision to treat a hypertensive individual should be based on the blood pressure level as well as the total cardiovascular risk and not on the blood pressure level alone[124 - 126].

Risk factors, target organ damage and associated clinical conditions

Studies have demonstrated the effects of a number of risk factors for heart disease divided into non-modifiable and modifiable[127 - 129]:

1. Non-Modifiable: age, gender, family history, and ethnicity.

2. Modifiable: High blood pressure, high serum cholesterol levels, tobacco smoking, excessive alcohol consumption, obesity, lack of physical activity, psychosocial factors, diabetes mellitus, and air pollution[130]. While the individual contribution of each risk factor varies between different communities or ethnic groups the consistency of the overall contribution of these risk factors to epidemiological studies is remarkably strong. Some of these risk factors, such as age, gender or family history, are immutable; however, many important cardiovascular risk factors are modifiable by lifestyle change, drug treatment or social change[131].

The major risk factors, target organ damage, and associated clinical conditions are shown in Table 3

Table 3: Major risk factors, TOD and ACC (Adapted from ESC/ESH Guidelines[132])

MAJOR RISK FACTORS.	TOD	ACC.
• Levels of systolic and diastolic BP. • Smoking. • Dyslipidaemia: o total cholesterol > 5.1 mmol/L, **OR** o LDL > 3 mmol/L, **OR** o HDL men < 1 and women < 1.2 mmol/L. • Diabetes mellitus. • Men > 55 years. • Women > 65 years. • Family history of early onset of CVD: o Men aged <55 years; o Women aged <65 years. • Waist circumference- abdominal obesity: o Men ≥ 94 cm; o Women ≥ 80 cm. The exceptions are South Asians and Chinese: Men: >90 cm and Women: >80 cm.	• LVH: based on ECG o Sokolow-Lyons > 38 mm; o Cornel > 2440 mm.ms) • Microalbuminuria: albumin creatine ratio 3-30 mg/mmol. • Slightly elevated creatinine: o men 115-133 µmol/L; o women 107-124 µmol/L	• Coronary heart disease. • Heart failure. • Chronic kidney disease: o albuminuria > 30mg/mmol **OR** o creatinine men > 133 µmol/L o creatinine women >124 µmol/L • Stroke or TIA. • Peripheral arterial disease. • Advanced retinopathy: o haemorrhages OR; o exudates; o papilloedema.

The decision to initiate therapy and the mode of treatment are influenced by the number of risk factors present, the target organ damage identified at evaluation and the associated clinical conditions present. Various regional and national Guidelines provide details in form of Risk stratification[132].

The new WHO guidelines for primary prevention of CVD recommend total cardiovascular risk assessment before making decisions on drug treatment including lipid-lowering therapy[133, 134].

Effect of lifestyle modifications

Table 4 shows the effect of lifestyle modifications on the systolic blood pressure.

Table 4: Effect of Lifestyle modification on SBP as recommended by JNC7[4]

Modifications*	**Recommendation**	**Approximate SBP reduction**
Reduce weight	Maintain normal body weight (BMI of 18.5 - 24.9 kg/m2)	3-20 mm Hg
Adopt DASH diet[130]	Rich in fruit, vegetables, and low-fat dairy; reduced saturated and total fat content	8–14 mm Hg
Reduce dietary sodium	<100 mmol (2.4 g)/day	2–8 mm Hg
Increase physical activity	Aerobic activity >30 min/day most days of the week	4 – 9 mmHg
Moderate alcohol consumption	Men: ≤ 2 drinks/day Women: ≤ 1 drink/day	2 – 4 mm Hg

*Combining 2 or more of these modifications may or may not have an additive effect on blood pressure reduction.
SBP = systolic blood pressure; BMI = body mass index; DASH = Dietary Approaches to Stop Hypertension
Chobanian AV, et al. JAMA. 2003;289:2560-2572;
Blumenthal JA, et al. Arch Intern Med. 2000;160:1947-1958

Drug Treatment

Hypertension is reversible, and several lines of evidence show that reducing BP affords cardiovascular protection, regardless of which antihypertensive drug is used. The BP Lowering Treatment Trialists' Collaboration performed a series of prospective overviews of numerous randomized trials that investigated the effects of different BP-lowering regimens on serious cardiovascular morbid and fatal events. These BP reductions were accompanied by significant reductions in primary outcomes, which included cardiovascular disease (18–22%), coronary heart disease (16–22%), and stroke (28–39%)[125 - 127].

The therapeutic goal should be to reduce blood pressure to less than140/90 mmHg for most individuals, and lower for those with diabetes or kidney disease (usual recommendation is to achieve levels below 120/80 mmHg) [135]. Guidelines on the choice of agents and how best to step up treatment for various subgroups have changed over time and differ between countries. No

consensus first line is agreed. While the Cochrane collaboration, World Health Organization and the United States guidelines support low dose thiazide-based diuretic as first line treatment[136 – 138], the UK guidelines emphasize calcium channel blockers (CCB) in preference for people over the age of 55 years or if of African or Caribbean family origin, with angiotensin converting enzyme inhibitors (ACE-I) used first line for younger people[139].

The majority of people require more than one drug to control their hypertension. JNC7[4] and ESH-ESC guidelines[132] advocate starting treatment with two drugs when blood pressure is >20 mmHg above systolic or >10 mmHg above diastolic targets. Most common combinations are renin–angiotensin system inhibitors and calcium channel blockers, or renin–angiotensin system inhibitors and diuretics[139]. Other combinations include calcium channel blockers and diuretics, beta-blockers and diuretics, dihydropyridine calcium channel blockers and beta-blockers, or dihydropyridine calcium channel blockers with either verapamil or diltiazem.

In spite of global improvement in the management of high blood pressure, control rates still remain significantly low due to certain impediments

Strategies for surmounting impediments to effective control

Table 5: Impediments and possible interventions (*Source: Siegel D: Vasc Health Risk Manag. 2005 March; 1(1): 9–14)*

Impediments	**Possible interventions**
Patient-based	
Attitudes about hypertension	Education at the community and individual level concerning consequences of hypertension
Medication side effects	Use of medications with fewer side effects
	Education of and treatment for sexual side effects
Medication cost	Use of diuretics and other generically available medication
Medication adherence	Less frequent dosing of medications, promotion of pillboxes, combination medications
	Methods to increase ease of medication renewal (ie, telephone or computer-linked)
	Rewards for higher adherence and lower blood pressure
Provider-based	
Knowledge	Conferences, academic detailing, computer-based algorithms, publication of clinical trials
Access	Use of physician extenders, group visits, work site care, expansion of health coverage
Awareness	Computer based reminders
Motivation	Incentives for health providers and managers
Societal-based	
Awareness	Public education campaigns
	Community-screening programs
	Work-based programs
Access to care	Expansion of health coverage (private and government financed)

Preventive strategies

The rising prevalence of hypertension worldwide calls for intensification of preventive measures. This is highly recommended for populations in the low- and medium income communities due to a looming explosion of cardiovascular morbidity and mortality. Important issues in hypertension prevention are:

- Patient education
- Screening for hypertension
- Primordial prevention
- Primary Prevention, and
- Secondary prevention.
- Improving Awareness

Primordial Prevention

- Primordial prevention of hypertension deals with addressing socio- cultural and socio-economic factors in the community that encourage the development of hypertension. Health policy makers and professionals should all be involved. Success would also be enhanced if community leaders and local chiefs are committed.
- Primordial prevention programmes should be part of local health policies for it to be sustained.

Primary Prevention

- Primary prevention of hypertension addresses the risk factors that favour the development of hypertension. Examples are: obesity, physical inactivity, excessive salt consumption etc. Community based programmes aimed at encouraging healthy lifestyles should be organized. Target groups e.g. school children; market women should be identified and used as focal points for the programmes. Individuals should be advised to maintain healthy lifestyles. Healthy eating with foods rich in fruits and vegetables should be recommended to the populace.
- **Secondary Prevention**
- Secondary prevention of hypertension refers to the management of the complications. It is necessary to intensify both primordial and primary prevention of hypertension in low- and medium economy settings. This is because the cost of managing the complications of hypertension in such environment could be enormous and beyond the reach of a majority of individuals. Adequate **follow-up** is advocated and this should be life-long even when blood pressures have been adequately controlled. At each visit, physical examination should be done and at least once yearly, detailed investigations to assess complications should be carried out. Any identified complication should be appropriately managed.

Role of International, Regional and National Organizations and Societies

International Organizations like the World Health Organization (WHO) and World Hypertension League (WHL) as well as Societies like the ISH collaborate in prevention of hypertension through encouraging research, organizing scientific meetings, workshops and arts competitions. The WHL in 2005 declared a 'World Hypertension Day' – an annual event to improve awareness

of hypertension. The ISH organizes hypertension programmes and teaching seminars in areas of high prevalence and low awareness globally.

Our contributions in the control of the scourge.

Our interest in hypertension stems for the desire to make our modest contributions to the control of a preventable scourge that is causing significant mortality and morbidity globally. The contributions have been in the areas of research and administration. Our research activities started with hospital based studies dating back to 1999 and continuing ever since[96, 101,141-148] mostly aimed at generating much needed data from our local institutions.

Drug trials for anti-hypertensive drugs were also carried out in collaboration with colleagues and associates[29, 32, 149, 150]. In 2005, we published a book on the management of hypertension[1] which is undergoing revision now.

The need to have hypertension management guidelines to take care of national and regional peculiarities stimulated our interest in being part of the publication of guidelines for hypertension in Sub-Saharan Africa (2003) and Nigeria (2005)[61, 78].

Recently, our interest shifted to epidemiological studies in search of the much needed local data on hypertension. This involved a market survey and community-based studies[59, 60, 62, 134, 151, 152] .

Apart from dedicated participation in hypertension research, we have been actively involved in local, national, and international hypertension society activities regularly attending annual scientific conferences with over 40 abstract presentations. We have also been at leadership positions in these Societies.

It should be pointed out that these contributions would not have been possible without the highly appreciated roles of my mentors, teachers, and friends who are appropriately acknowledged later during this lecture.

CONCLUSIONS

I would conclude this lecture by a quote from the United Nation's Secretary-General, Ban Ki-moon in response to a question by the Global International on his vision for the new year 2013.

"We stand at a critical crossroads in history when our actions – or inaction – can shape the future of life on Earth as we know it.……

….. This is a global challenge, one requiring global cooperation among all sectors of society. In the coming year, my hope is that governments, working with the business community, civic organizations, foundations, academic and faith based groups, will continue to work with the United Nations to help forge a more sustainable path to the future. Working together, we can bring hope and opportunity to all. The future is truly in our hands."

This statement can aptly be applied to the hypertension scourge which is indeed a global challenge that needs all of us and all *Nations* to *Unite* in combating the albatross.

ACKNOWLEDGEMENT

I thank the Almighty God who created man and bestowed him with knowledge and wisdom to surmount challenges strewn along the pathway of his life's journey, among other reasons, to lessen boredom.

I thank the Vice Chancellor, Professor Batho Okolo and the University administration for ensuring the success of today's event. I specially thank Professor Chinedu Nebo, immediate past Vice Chancellor for touching lives of staff and students and providing the firm academic framework maintained and upgraded infra-structurally and internationally by the current administration. I appreciate the dedication to duties of the Chairman, Senate Ceremonials Committee, Professor Obi Njoku and the members of that Committee.

My family members, nuclear and extended – the entire Onwubere family, the Aguta and Onyekuru families, and all friends and associates for being there for me all the time. My immediate family members who continue to cope with my periodic absence from home attending conferences or attending to clients sometimes into late hours are highly appreciated.

I wish to pay tribute to my mentors who stimulated and sustained my interest in Hypertension notably Professor Emeritus Oladipo Akinkugbe, the Father of Hypertension in Africa and Nigeria whom I have learnt a lot from over the years. I have also trailed behind him (at a safe distance) in the hypertension story nationally and internationally. Professor Emeritus Yackoob Seedat, another Father of Hypertension in Africa who has also been a father to me at the international arena. YK ensured my nomination to sit on the Scientific Council of the International Society of Hypertension after his two-term tenure four years ago. I appreciate my colleagues and collaborators in cardiovascular medicine within the Country – Professors Solo Kadiri, Austin Obasohan, James Odia, Clement Odigwe, Basil Okeahialam and a host of others.

Without the tutelage and special care of my Teachers at various stages of my education, I would not be giving this lecture today. I would just mention one per education stage as point of contact to represent the rest – Mr Goddy Kamalu (my Standard 6 Teacher), Mr J A Garrod (my Principal at Government Secondary School, Owerri), and Professor Chukwuedu Nwokolo (representing my University Teachers). I remain grateful to them for shaping my future.

The Department of Medicine has been a source of inspiration to me. Among those who at one time or the other guided me on the path of my career path include Professors Johnny Oli, Dede Iheanacho, Vincent Ikeh, Eddy Okoroma and others. Professor Sam Ike (Venerable of the Anglican Church) deserves special mention. A relationship that started with me as his academic/professional supervisor has grown into a situation of mutual trust and confidence. He did proof-read not only this script but also a book publication I made 8 years ago. I thank him and his wife who also participated actively in the logistics of this Lecture. Dr. Emmanuel Ejim has been and remains my professional son right from his days as a medical student. He has been

highly reliable and ever there for me in both official, private and family capacities. The recent passing on of his dear spouse at a time finishing touches were being put on this Inaugural Lecture pained me immensely. (May Chinelo's soul rest in perfect peace. Amen). I love all staff of my department – academic and administrative for the cohesion and friendship that exists in that family.

I learnt a great deal from and remain appreciative of late Professor John Goodwin, Dr. Celia Oakley and others at the Royal Postgraduate Medical College/ Hammersmith Hospital, London where I had part of my postgraduate programme between January, 1981 and May, 1983.

I appreciate in a special way, the entire College of Medicine staff for their un-alloyed support these past few years. The College academic community have consistently reposed great confidence in my administrative capacity in spite of obvious challenges while the administrative staff, especially Principal Officers of the College of Medicine have not quivered in their co-operation.

I thank all who are here today, Your Lordships, Your Excellencies, and distinguished ladies and gentleman for giving me this honour today. May God bless you all abundantly and grant you safe journey back home.

Finally, the Inaugural Committee members contributed tremendously to the successful event today and deserve mention - Profs. Ifeoma Ulasi and Sam Ike; Drs. Chuba Ijoma, Ben Anisiuba, Sylvester, Nwokediuko,Emma Ejim, Chinwe Onyekonwu, Raph Anakwue, Oluchi Ekenze, Ekene Young, and Esther Ekwe; Mrs. Ngozi Uzoagba, and Mrs. Becky Anyanwu. God bless you all.

REFERENCES

1. **Onwubere BJC** (ed). Management of Hypertension. 2005. Institute of Development Studies, University of Nigeria.
2. Guidelines Sub-Committee. 1999 World Health Organization – International Society of Hypertension guidelines for the management of hypertension. J Hypertens. 1999;17: 151-183.
3. World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens. 2003;21:1983-1992
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The Seventh Report of the Joint national Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. JAMA 2003; 289:2560–2572.
5. De la Sierra A. Blood pressure control in the hypertensive population. What else the doctor can do? Journal of Hypertension 2010; 28:1129–1130
6. Nei Ching. Y*ellow Emperor's Classic of Internal Medicine*. Books 2–9 published between 2698 and 2598 B.C

7. Esunge PM. From blood pressure to hypertension: the history of research. J R Soc Med. 1991; 84 (10): 621
8. Kotchen TA. Historical trends and milestones in hypertension research: a model of the process of translational research. Hypertension. 2011; 58 (4): 522–538.
9. Harvey W. On the Motion of the Heart and Blood in Animals. 1889; London: George Bell and Sons
10. Hall WD. Stephen Hales: theologian, botanist, physiologist, discoverer of haemo-dynamics. Clinical Cardiology. 1987; 10 (8): 487–489
11. Swales JD, ed. Manual of hypertension. Oxford: Blackwell Science.1995; pp. xiii. ISBN 0-86542-861-1.
12. Postel-Vinay N, ed. A century of arterial hypertension 1896–1996. Chichester: Wiley. 1996; p. 213. ISBN 0-471-96788-2.
13. Hajjar I, Kotchen TA . Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. JAMA. 2003;290(2):199-206.
14. Keith NM, Wagener HP, Kernohan JW. The syndrome of malignant hypertension. Arch. Intern. Med. 1928; 41 (2): 141–188.
15. Hay JH. A British Medical Association Lecture on THE SIGNIFICANCE OF A RAISED BLOOD PRESSURE. Br. Med. J. 1931; 2 (3679): 43–47.
16. White PD. Heart Disease (2nd ed.). New York, NY: MacMillan Co. 1937; p. 326.
17. Bruenn HG. Clinical notes on the illness and death of president Franklin D. Roosevelt. Ann. Int. Med. 1970; 72 (4): 579–591.
18. Friedberg CK. Diseases of the Heart. Philadelphia, PA: WB Saunders Co. 1949.
19. Moser M. Historical perspectives on the management of hypertension. J. Clin. Hypertens. 2006; 8 (8 Suppl 2): 15–20.
20. "Section 30: Some characteristics related to the incidence of cardiovascular disease and death: 18 year follow-up". The Framingham Study; DHEW Publication No. (NIH) 74-599. Bethesda, MD: National Heart and Lung Institute. 1974
21. Society of Actuaries Committee on Mortality. Build and blood pressure study, 1959. Chicago, IL: Society of Actuaries. 1960.
22. Dustan HP, Roccella EJ, Garrison HH. Controlling hypertension. A research success story. Arch. Intern. Med. 1996;156 (17): 1926–1935
23. Novello FC, Sprague JM. Benzothiadiazine dioxides as novel diuretics. J. Am. Chem. Soc. 1957;79 (8): 2028
24. Freis ED, Wanko A, Wilson IM, et al. Treatment of essential hypertension with chlorothiazide (diuril); its use alone and combined with other antihypertensive agents. J Am Med Assoc 1958;166: 137–140.
25. Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. JAMA 1970;213: 1143–1152.
26. Freis ED The Veterans Administration Cooperative Study on Antihypertensive Agents. Implications for Stroke Prevention. Stroke 1974; 5 (1): 76–77.
27. Giles T, Aranda JM Jr, Suh DC, Choi IS, Preblick R, Rocha R, Frech-Tamas F. Ethnic/racial variations in blood pressure awareness, treatment, and control.. J Clin Hypertens (Greenwich). 2007; 9(5):345-354.
28. Ondetti MA, Rubin B, Cushman DW . Design of specific inhibitors of angiotensin-converting enzyme: new class of orally active antihypertensive agents. Science April 1977; 196 (4288): 441–444.
29. **Onwubere BJC**, Ike SO, Asiegbu P, Nlemadim M, Umeh RE. Comparison of the efficacy, safety and tolerability of Tritace® (Ramipril) with Amlodipine In treatment of mild to moderate hypertension In Nigerians seen at the University of Nigeria Teaching Hospital, Enugu. J Coll of Medicine 2007; 12(2):93-98.
30. Wexler RR, Greenlee WJ, Irvin JD, et al. (February 1996). "Nonpeptide angiotensin II receptor antagonists: the next generation in antihypertensive therapy". J. Med. Chem. 39 (3): 625–656
31. Jensen C, Herold P, Brunner HR (May 2008). "Aliskiren: the first renin inhibitor for clinical treatment". Nat Rev Drug Discov 7 (5): 399–410

32. **Onwubere BJC** , Ijoma CK, Anisiuba BC. Efficacy, tolerability and safety of Valsartan In patients with mild to moderate Essential Hypertension treated at the University of Nigeria Teaching Hospital, Enugu: Nigerian Medical Practitioner. 2006; 50(2): 27- 32
33. Freis E. A history of hypertension treatment. In: Oparil S, Weber MA eds. Hypertension: Companion to Brenner & Rector's The Kidney. 2nd ed. Philadelphia, PA: Elsevier/Saunders; 2005: 1–6(chapter 1)
34. Ambard L, Beaujard C. Causes de l'hypertension arterielle. Arch Gen Med. 1904; 1:520 –533.
35. Kotchen TA. Historical trends and milestones in hypertension research: a model of the process of translational research. Hypertension. 2011;58: 522-538.
36. Boegehold M, Kotchen TA. Importance of dietary chloride for salt sensitivity of blood pressure. Hypertension. 1991;17:I158 –I161
37. Kempner W. Treatment of hypertensive vascular disease with rice diet. Am J Med. 1948;4: 545–576
38. Pickering G. The therapy of hypertension: object and methods. In: Pickering G, ed. High Blood Pressure. 2nd ed. New York, NY: Grune & Stratton; 1968:392.
39. Langford HG, Blaufox MD, Oberman A, Hawkins CM, Curb JD, Cutler GR, Wassertheil-Smoller S, Pressel S, Babock C, Abernethy JD, Hotchkiss J, Tyler M. Dietary therapy slows the return of hypertension after stopping prolonged medication. JAMA. 1985; 253: 657– 664.
40. Langford HG, Davis BR, Blaufox D, Oberman A, Wassertheil-Smoller S, Hawkins M, Zimbaldi N. Effect of drug and diet treatment of mild hypertension on diastolic blood pressure: the TAIM Research Group. Hypertension. 199;17: 210 –217.
41. The effects of non-pharmacologic interventions on blood pressure of persons with high normal levels. Results of Trials of Hypertension Prevention, Phase I. JAMA. 1992; 267: 1213–1220.
42. Schneider RH, Staggers F, Alexander CN, Sheppard W, Rainforth M, Kondwani K, Smith S, King CG. A randomized controlled trial of stress reduction for hypertension in older African Americans. Hypertension. 1995; 26: 820–827.
43. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure: DASH Collaborative Research Group. N Engl J Med. 1997; 336:1117–1124.
44. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WH Jr, Kostis JB, Kumanyika S, Lacy CR, Johnson KC, Folmar S, Cutler JA. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of non-pharmacologic interventions in the elderly (TONE)– TONE Collaborative Research Group. JAMA. 1998;279–839-846.
45. Stevens VJ, Obarzanek E, Cook NR, Lee IM, Appel LJ, Smith West D, Milas NC, Mattfeldt-Beman M, Belden L, Bragg C, Millstone M, Raczynski J, Brewer A, Singh B, Cohen J, for the Trials for Hypertension Prevention Research Group. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention phase II. Ann Intern Med. 2001; 134 :1–11.
46. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer P, Stevens VJ, Vollmer WM, Lin PH, Svetkey LP, Stedman SW, Young DR, for the Writing Group of the PREMIER Collaborative Research Group. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA. 2003;289: 2083–2093.
47. Donnison C. Blood pressure in the African natives: its bearing upon aetiology of hyperpiesa and arteriosclerosis. Lancet. 1929;1: 6 –7.
48. Opie LH, Seedat YK. Hypertension in Sub-Saharan African Populations. Circulation 2005; 112:3562–3568
49. Akinkugbe O. World epidemiology of hypertension in blacks. In: Hall W, ed. Hypertension in Blacks: Epidemiology, Pathophysiology, and Treatment. Chicago: Year Book Medical Publishers; 1985:13–16.
50. Cappuccio FP, Micah FB, Emmett L, Kerry SM, Antwi S, Martin-Peprah R, Phillips RO, Plange-Rhule J, Eastwood JB. Prevalence, detection, management, and control of hypertension in Ashanti, West Africa. Hypertension. 2004;43:1017–1022.

51. Pobee JO, Larbi EB, Belcher DW, Wurapa FK, Dodu SR. Blood pressure distribution in a rural Ghanaian population. Trans R Soc Trop Med Hyg. 1977;71: 66 –72.
52. Oviasu VO. Arterial blood pressures and hypertension in a rural Nigerian community. Afr J Med Med Sci. 1978;7:137–143.
53. Mokhobo KP. Arterial hypertension in rural societies. East Afr Med J. 1976;53: 440–444.
54. Seedat YK, Seedat MA, Hackland DB. Prevalence of hypertension in the urban and rural Zulu. J Epidemiol Community Health. 1982;36: 256 –261.
55. Mensah GA. Epidemiology of stroke and high blood pressure in Africa. Heart 2008;94:697–705
56. Edwards R, Unwin N, Mugusi F, et al. Hypertension prevalence and care in an urban and rural area of Tanzania. J Hypertens 2000;18:145–152.
57. Addo J, Amoah AG, Koram KA. The changing patterns of hypertension in Ghana: a study of four rural communities in the Ga District. Ethn Dis 2006;16:894–899.
58. Akinkugbe OO. The Nigerian hypertension programme. J Hum Hypertens 1996;10(Suppl 1):S43–6.
59. **Onwubere BJC**, Ejim EC, Okafor CI, Emehel IA, Mbah AU, Onyia U, Mendis S. Pattern of Blood Pressure Indices among the Residents of a Rural Community in South East Nigeria. International Journal of Hypertension., Article ID 621074, 6 pages.
60. Ulasi II, Ijoma CK, **Onwubere BJC**, Arodiwe E, Onodugo O, Okafor C High Prevalence and Low Awareness of Hypertension in a Market Population in Enugu, Nigeria. International Journal of Hypertension. (2011), Article ID 869675, 5 pages
61. Lemogoum D, Seedat YK, Mabadeje AFB, **Onwubere BJC**, et al. Recommendations for prevention, diagnosis and management of hypertension and cardiovascular risk factors in sub-Saharan Africa. Journal of Hypertension 2003; 21: 1-8
62. Ogah OS, Okpechi I, Chukwuonye II, Akinyemi JO, **Onwubere BJC**, Falase AO, Stewart S, Sliwa K. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: A review. World J Cardiol 2012; 4(12): 327-340
63. Callander WH. Blood pressure in Nigerian soldiers and army recruits. West Afr Med J 1953; 2: 2-103
64. Nwokolo C. Endomyocardial fibrosis and other obscure cardiopathies in eastern Nigeria. West Afr Med J 1955; 4: 103-116
65. Beet EA. Rheumatic heart disease in Northern Nigeria.Trans R Soc Trop Med Hyg 1956; 50: 587-592
66. Abrahams DG, Alele CA, Barnard BG. The systemic blood pressure in a rural West African community. West Afr Med J 1960; 9: 45-58
67. Akinkugbe OO, Brown WC, Cranston WI. Pressor effects of angiotensin infusions into different vascular beds in the rabbit. Clin Sci 1966; 30: 409-416
68. Akinkugbe OO, Brown WC, Cranston WI. The direct renal action of angiotensin in the rabbit. Clin Sci 1966; 30: 259-266
69. Akinkugbe OO, Brown WC, Cranston WI. Response to angiotensin infusion before and after adrenalectomy in the rabbit. Am J Physiol 1967; 212: 1147-1152
70. Akinkugbe OO. The rarity of hypertensive retinopathy in the African. Am J Med 1968; 45: 401-404
71. Akinkugbe OO, Jaiyesimi F. The rarer causes of hypertension in Ibadan. (An eleven-year study). West Afr Med J Niger Pract 1968; 17: 82-85
72. Akinkugbe OO. Hypertensive disease in Ibadan, Nigeria. A clinical prospective study. East Afr Med J 1969; 46: 313-320
73. Akinkugbe OO. School survey of arterial pressure and proteinuria in Ibadan, Nigeria. East Afr Med J 1969; 46: 257-261
74. Akinkugbe OO. Antihypertensive treatment in the African context. Practitioner 1969; 202: 549-552
75. Akinkugbe OO, Carlisle R, Olatunde IA. Proceedings: Beta-adrenergic blockers in the treatment of hypertension: experience with propranolol at the U.C.H. Ibadan, Nigeria. West Afr J Pharmacol Drug Res 1974; 2: 63P-64P

76. Akinkugbe OO, Akinkugbe FM, Ayeni O, Solomon H, French K, Minear R. Biracial study of arterial pressures in the first and second decades of life. Br Med J 1977; 1: 1132-1134.
77. Ladipo GO. Hypertensive retinopathy in Nigerians. A prospective clinical study of 350 cases. Trop Geogr Med 1981; 33: 311-316
78. **Onwubere BJC**, Kadiri S (Eds). Guidelines for the Management of Hypertension in Nigeria.). Ezu Books Limited.2005
79. Carretero OA, Oparil S. "Essential hypertension. Part I: definition and etiology". Circulation 2000; 101(3): 329–335.
80. Hall JE, Guyton AC (eds). Textbook of medical physiology. 2006. St. Louis, Mo: Elsevier Saunders. pp. 228. ISBN 0-7216-0240-1
81. Gandhi SK, Powers JC, Nomeir AM, Fowle K, Kitzman DW, Rankin KM, et al. The pathogenesis of acute pulmonary edema associated with hypertension. N Engl J Med. Jan 4 2001;344(1):17-22
82. Klabunde R (ed) Cardiovascular Physiology Concepts. (2005). Lippincott Williams & Wilkins. pp. 93–4. ISBN 978-0-7817-5030-1.
83. Carretero OA, Oparil S. "Essential hypertension. Part I: definition and etiology". Circulation 2000; 101(3): 329–335.
84. Levy D, DeStefano AL, LarsonMG, O'Donnell CJ, Lifton RP, Gavras H, et al.Evidence for a gene influencing blood pressure on chromosome 17. Genome scan linkage results for longitudinal blood pressure phenotypes in subjects from the Framingham Heart Study. Hypertension 2000; 36:477– 483.
85. Tobin MD, Raleigh SM, Newhouse S, Braund P, Bodycote C, Ogleby J, et al. Association of WNK1 gene polymorphisms and haplotypes with ambulatory blood pressure in the general population. Circulation 2005; 112:3423–3429.
86. Page LB, Damon A, Moellering RC Jr. Antecedents of cardiovascular disease in six Solomon Islands societies. Circulation. 1974;49: 1132–1146.
87. Page IH. The mosaic theory. In: Page IH, ed. Hypertension Mechanisms. New York, NY: Grune & Stratton: 1987:910–916.
88. Guyton AC. The body's approach to arterial pressure regulation. In: Guyton AC, ed. Arterial Pressure and Hypertension. Philadelphia, PA: WB Saunders Co; 1980:1–9 (chapter 1).
89. Brunner HR, Laragh JH, Baer L, Newton MA, Goodwin FT, Krakoff LR, Bard RH, Buhler FR. Essential hypertension: renin and aldosterone, heart attack and stroke. N Eng J Med. 1972;286: 441– 449.
90. Navar LG. Counterpoint: Activation of the intrarenal renin-angiotensin system is the dominant contributor to systemic hypertension. J. Appl. Physiol. 2010; 109 (6): 1998–2000.
91. Esler M, Lambert E, Schlaich M. Point: Chronic activation of the sympathetic nervous system is the dominant contributor to systemic hypertension. J. Appl. Physiol. 2010; 109 (6): 1996–1998.
92. Versari D, Daghini E, Virdis A, Ghiadoni L, Taddei S. Endothelium-dependent contractions and endothelial dysfunction in human hypertension. Br. J. Pharmacol. 2009; 157 (4): 527–536.
93. Marchesi C, Paradis P, Schiffrin EL. Role of the renin-angiotensin system in vascular inflammation. Trends Pharmacol. Sci. 2008; 29 (7): 367–374.
94. Steinmetz M, Nickenig G. "[Cardiac sequelae of hypertension]". Der Internist. 2009; 50 (4): 397–409.
95. Lip GY, Felmeden DC, Li-Saw-Hee FL, Beevers DG. Hypertensive heart disease. A complex syndrome or a hypertensive 'cardiomyopathy'?. Eur Heart J. 2000; 21 (20): 1653–1665
96. Ike SO, **Onwubere BJC**: Relationship between Diastolic Dysfunction and level of blood pressure in Blacks. Ethnicity and Disease, 2003;13(4): 463 – 469
97. Ogah OS, Akinyemi RO, Adegbite GD, Udofia OI, Udoh SB, Adesina JO, et al. Prevalence of asymptomatic left ventricular systolic dysfunction in hypertensive Nigerians: echocardiographic study of 832 subjects. Cardiovasc J Afr 2011; 22: 297-302
98. Ike SO, **Onwubere BJC**, Okwara CC. Acute myocardial infarction presenting in a woman with multiple cardiovascular risk factors.: case Report. West African Journal of Radiology. 2009; 16(1): 40 – 44.

99. Anjorin CO, Buba F, Eneh AC. Myocardial infarction at the University of Maiduguri Teaching Hospital, North Eastern Nigeria: A long term review. J Med Sci 2005; 5: 358-362
100. **Onwubere BJC**, Ike SO Review of Medical Admissions at the University of Nigeria Teaching Hospital, Enugu.. Nigerian Journal of Internal Medicine. 1999;.2 (2): 59-62.
101. **Onwubere BJC**, Ike SO Prevalence of Hypertension and its Complication Among Medical Admissions At The University Of Nigeria Teaching Hospital, Enugu. Nigerian Journal of Internal Medicine: 2000 Vol.3 No.1 17-20
102. Ike SO. Prevalence of hypertension and its complications among medical admissions at the University of Nigeria Teaching Hospital, Enugu (Study 2). Niger J Med 2009; 18: 68-72
103. Arodiwe EB, Ike SO, Nwokediuko SC. Case fatality among hypertension-related admissions in Enugu, Nigeria. Niger J Clin Pract 2009; 12: 153-156
104. Ukoh VA. Admission of hypertensive patients at the University of Benin Teaching Hospital, Nigeria. East Afr Med J 2007; 84: 329-335
105. Onwuchekwa AC, Asekomeh EG, Iyagba AM, Onung SI. Medical mortality in the Accident and Emergency Unit of the University of Port Harcourt Teaching Hospital. Niger J Med 2008; 17: 182-185
106. White WB. Defining the problem of treating the patient with hypertension and arthritis pain. The American Journal of Medicine. 2009; 122 (5 Suppl): S3–S9.
107. Sare GM, Geeganage C, Bath PM. High blood pressure in acute ischaemic stroke--broadening therapeutic horizons. Cerebrovascular Diseases. 2009; 27 Suppl 1: 156–161.
108. Ogun SA, Ojini FI, Ogungbo B, Kolapo KO, Danesi MA. Stroke in south west Nigeria: a 10-year review. Stroke 2005; 36: 1120-1122
109. Osuji CU, Nwaneli CU, **Onwubere BJ**, Onwubuya EI, Ahaneku GI. Renal function in patients with hypertension associated congestive cardiac failure seen in a tertiary hospital. International Journal of Nephrology. Volume 2012, Article ID 769103. doi: 10.1155/2012/769103
110. Ulasi II, Ijoma CK. The enormity of chronic kidney disease in Nigeria: the situation in a teaching hospital in South-East Nigeria. J Trop Med 2010; 2010: 501957
111. Wong TY, Mitchell P. Hypertensive retinopathy. The New England Journal of Medicine. 2004; 351 (22): 2310–2317
112. Kearney PM, Whelton M, Reynolds K, Munter P, Whelton PK, He J: Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365:217-223.
113. World Health Organization: World Health Report 2002. Reducing risks, promoting healthy life. 2002 [http://www.who.int/whr/ 2002/en/index.html]. Geneva: WHO
114. WHO AFRO: Cardiovascular diseases in the African Region: Current Situation and Perspectives. Report of the Regional Director. Fifty-fifth session. 2005 [http://www.afro.who.int/rc55/ documents/afr_rc55_12_cardiovascular.pdf]. Maputo, Mozambique
115. Cooper RS, Amoah AG, Mensah GA: High blood pressure: the foundation for epidemic cardiovascular disease in African populations. Ethn Dis 2003; 13:s48-s52.
116. Kearney PM, Whelton M, Reynolds K, Munter P, Whelton PK, He J: Worldwide prevalence of hypertension: a systematic review. J Hypertens 2004; 22:11-19.
117. Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. Lancet. 2007; 370: 1929–1938.
118. Sliwa K,Stewart S, Gersh BJ. Hypertension: A Global Perspective. Circulation. 2011;123:2892-2896
119. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, World Health Organization, 2009 (http://www.who.int/healthinfo/global_burden_disease/ GlobalHealthRisks_report_full.pdf).
120. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, et al. National, regional, and global trends in systolic blood pressure since 1980: Systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. Lancet, 2011; 377:568–577.

121. Global Health Observatory. Geneva, World Health Organization, 2011 (http://www.who.int/gho).
122. Twagirumukizaa M, De Bacquerb D, Kipsc JG, de Backerb G, Stichelec RV, Van Bortel LM. Current and projected prevalence of arterial hypertension in sub-Saharan Africa by sex, age and habitat: an estimate from population studies. Journal of Hypertension 2011, 29:1243–1252
123. World Health Statistics 2012. Geneva, World Health Organization, 2012
124. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies: Prospective Studies Collaboration. Lancet. 2002; 360: 1903-1912.
125. Mancia G. Defining blood pressure goals: is it enough to manage total cardiovascular risk? Journal of Hypertension 2009; 27 (suppl 5):S3–S8
126. Turnbull F, Neal B, Algert C, Chalmers J, Chapman N, Cutler J, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med. 2005; 165:1410–1419.
127. Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Lancet 2003; 362:1527–1535.
128. Kelly BB; Fuster V. Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health. Washington, DC. 2010: National Academies Press. ISBN 0-309-14774-3.
129. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364 (9438): 937–952.
130. Blumenthal JA, Babyak MA, Hinderliter A et al. Effects of the DASH diet alone and in combination with exercise and weight loss on blood pressure and cardiovascular biomarkers in men and women with high blood pressure: the ENCORE study. Arch. Intern. Med. 2010; 170 (2): 126–135.
131. Greenhalgh J, Dickson R, Dundar Y. The effects of biofeedback for the treatment of essential hypertension: a systematic review. Health Technol Assess. 2009; 13 (46): 1–104.
132. Mancia G, Laurent S, Agahiti-Rosei, et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force Document. J Hypertens 2009; 27: 2121 – 2158
133. World Health Organization. Prevention of cardiovascular disease: guidelines for assessment and management of total cardiovascular risk. Geneva, Switzerland: WHO; 2007.
134. Mendis S, Lindholm LH, Anderson SG, Alwan A, Koju R, **Onwubere BJC**, et al Total cardiovascular risk approach to improve efficiency of cardiovascular prevention in resource constrain settings Journal of clinical epidemiology. 2011; 64(12): 1264 – 1474
135. Nelson M. Drug treatment of elevated blood pressure. (http:/ / www. australianprescriber. com/ magazine/ 33/ 4/ 108/ 12). Australian Prescriber (33): 108–112. . Retrieved August 11, 2010.
136. Klarenbach SW, McAlister FA, Johansen H, Tu K, et al. Canadian Hypertension Education,Program. Identification of factors driving differences in cost effectiveness of first-line pharmacological therapy for uncomplicated hypertension. The Canadian journal of cardiology. 2010; 26 (5): e158–e163.
137. Wright JM, Musini VM. Wright, James M. ed. "First-line drugs for hypertension". Cochrane Database Syst Rev (3): 2009. PMID 19588327.
138. Okonofua EC, Simpson KN, Jesri A, Rehman SU et al. Therapeutic Inertia Is an Impediment to Achieving the Healthy People 2010 Blood Pressure Control Goals" (http:/ / hyper. ahajournals. org/ cgi/ content/ abstract/ 47/ 3/ 345). Hypertension . 2006; 34: 345–351.
139. Sever PS, Messerli FH. Hypertension management 2011: optimal combination therapy. Eur. Heart J. 2011; 32 (20): 2499–2506.
140. Egan BM, Basile JN. Controlling blood pressure in 50% of all hypertensive patients: an achievable goal in the healthy people 2010 report? J Invest Med. 2003;51:373–385.

141. Ogbu ISI, Udoh AE, Etukudo MH, **Onwubere BJC**. Metabolic syndrome in Nigerian hypertensive subjects: risk factor analysis. Global Journal of Medical Sciences, Vol 9, No 1&2 (2010)
142. Onwamaeze IC, Okereke SN, **Onwubere BJC**, Ezeoke ACJ Serum Cations in Hypertensive Nigerians. Nigerian Journal of Internal Medicine. 1999; 2(3/4): 83-85.
143. Ike SO, Anisiuba BC, **Onwubere BJC**, Ikeh VO Clinic Attendance Compliance Pattern of Adult Hypertensive Nigerians seen at the UNTH, Enugu., Orient Medical Journal: 2003; 15 (3/4): 1-7
144. Nkado RN, **Onwubere BJC**, Ikeh VO, Anisiuba BC. Correlation of Electrocardiogram with Echocardiographic left ventricular mass in adult Nigerians with systemic hypertension. West African Journal of Medicine 2003;22(3): 206 –210.
145. Ike SO, Anisiuba BC, **Onwubere BJC**, Ikeh VO Initial antihypertensive therapy: prescription pattern at the out-patient Cardiology clinic of the University of Nigeria Teaching Hospital (UNTH), Enugu.. Journal of College of Medicine 2006; 2(1):8 - 14
146. Ejezie FE, Onwusi EA, **Onwubere BJC**. Blood glucose levels in hypertensive patients at the cardiac clinic of the university of Nigeria teaching hospital, Enugu, Nigeria.. J Medical Research and Technoology. 2005; 2(1): 18
147. **Onwubere BJC**, Onwamaeze IC Serum electrolytes, urea, and creatinine in hypertensive Nigerians. J Medical Research and Technoology. 2005. Vol 2 (1): 4 -14.
148. Ejim EC, Ike SO, Anisiuba BC, Essien IO, **Onwubere BJ**, Ikeh VO. Cardiac Arrhythmias in Recently Diagnosed Hypertensive Patients at First Presentation an Electrocardiographic-Based Study. Nig Journal of Medicine. 2012; 21(1): 6 – 10.
149. **Onwubere BJC**, Obodo JO, Oke DA, Okeahialam BN, Danbauchi S and Mbakwem AC. A Randomised trial to Compare the Efficacy and Safety of Felodipine and Nifedipine in patients with mild to moderate Hypertension.: West African Journal of Medicine 2001; 20(4).
150. **Onwubere BJC**, Ohaju-Obodo JO, Ike SO Assessment of the effects of nisoldipine in patients with mild to moderate hypertension. Orient Medical Journal.2005; 17(3/4):11 - 16
151. Ejim EC, Okafor CI, Emehel A, Mbah AU, Onyia U, Egwuonwu T, Akabueze J**, Onwubere BJ.** Prevalence of Cardiovascular Risk Factors in a Nigerian Rural Community, J. Trop. Med. 2011 Article ID 308687, 6 pages
152. Ogah OS, Madukwe OO, Chukwuonye II, Onyeonoro UU, Ukaegbu AU, Akhimien MO, **Onwubere BJC**, Okpechi IG.Prevalence and determinants of hypertension in Abia State Nigeria: Results from the Abia State Non-Communicable diseases and Cardiovascular Risk factors Survey. Ethn Dis 2012. (Accepted 11 Jan 2013)