THERAPEUTIC PROTOCOL OF HYPERTENSION MANAGEMENT IN ABU TEACHING HOSPITAL, ZARIA: A 12-MONTH RETROSPECTIVE STUDY (NOVEMBER 1997- NOVEMBER 1998)

BY

FATIMAH BINTA YUSUF

A CLINICAL THESIS SUBMITTED TO THE DEPARTMENT OF PHARMACOLOGY AND CLINICAL PHARMACY, FACULTY OF PHARMACEUTICAL SCIENCES , AHMADU BELLO UNIVERSITY, ZARIA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE, PHARMACOLOGY (M.SC PHARMACOLOGY)

JUNE, 2000

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DECLARATION

I hereby declare that this thesis was written by me and that it is a record of my own research work. To the best of by knowledge, this thesis has not been presented to any postgraduate school for the award of a higher degree.

Fatimah B. Yusuf

Dec. 12, 2000
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DEDICATION

To my best friend, my Husband, Alhaji Abubakar Shehu Yusuf, for his **total** support and loving encouragement.

To the future generation of African Women in Science and Technology: our Daughters and Sisters. In recognition of the choices they see us make everyday, and which they will have to make: Studying to any level, holding responsible jobs, becoming wives and mothers, and juggling all roles with success.

CERTIFICATION

This thesis entitled "The therapeutic Protocol of Hypertension Management in A.B.U. Teaching Hospital, Zaria". A 12 month retrospective study (November 1997 to November, 1998) by FATIMA BINTA YUSUF meets the regulations governing the award of the degree of Master of Science (M.Sc.) Pharmacology of Ahmadu Bello University and is approved for its contribution to knowledge and literary presentation.

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ABSTRACT

Hypertension or high blood pressure has been described by the world Health Organisation (WHO), expert committee on arterial hypertension as, "the persistent elevation of arterial blood pressure". (4)

Hypertension is a very common condition which if untreated increases the risk of complications (such as heart attack, stroke, kidney failure and retinal damage) and decreases life expectancy.

Therefore, good management and control, as promoted by WHO are required. A necessary step to be taken is to adhere to a good therapeutic protocol in the management and control of hypertension. This protocol covers the choice of effective antihypertensive drugs, prescriber preferences as well as patient perception and satisfaction, which serve as important indicators of certain aspects of the complex process of hypertension control and management.

The benefits to be derived from good and effective management of hypertension include prevention of morbid and fatal cardiovascular and renal events, improvement in the quality of life gained by avoiding hospital admission and reduction in the need for rehabilitation.

programme to study therapeutic protocol of hypertension management may take any of several approaches as described by the WHO. ([233)] The patient approach

was used in this study. It involved selection of a sample of patients with established hypertension. These patients were interviewed and their case histories were reviewed as well. This is called a retrospective assessment.

In this study, five (5) evaluative criteria were surveyed using both patient records and questionnaires, personal data, family, social, clinical and drug histories were surveyed as well as non-drug therapeutic measures used in the management of hypertension, for the period of this study, (November 1997 to November 1998), in Ahmadu Bello University Teaching Hospital, ABUTH, Zaria.

The exclusion criterion was that newly diagnosed hypertensive patients were not selected and only those known hypertensive patients that attended the cardiac clinic during the period of the survey were selected.

41 hypertensive patients were studied (hypertension prevalence has a normal distribution in the population and a sample can be used to study the whole population). There were more female sufferers of hypertension (76%). Hypertension was highest between 41 - 69 years in female and between 50 - 70 years in male patients. Many patients were obese (31%). Female patients were either housewives or petty traders (36%) Male patients had varied occupations. There was no parental history of hypertension in (70%) of patients while (15%) had hypertensive fathers and (15%) had hypertensive mothers. Among some female patients hypertension was pregnancy related. The prevalence of pregnancy - induced hypertension was (43%) while 17% of cases were pregnancy - aggravated.

Few patients (7%) were found to consume alcohol and the prevalence of cigarette smoking was (17%), while Kolanut comsuption was (70%), and addition of salt at table was (56%), while potash consumption was found to be (88%).

The average age at diagnosis was 31 to 50 years (43.28+-x= 12.8). Incidence of co-existing illness for example was low (34%). Presenting complaints mostly involved the nervous system (45%), the cardiovascular system (20%) and the respiratory system which was 12%.

Prescription at diagnosis mostly contained diuretics (41%) followed by the centrally - acting drug methyldopa (17%). This trend changed slightly (after four months) to show in the current prescriptions that the first line drugs was still the diuretic agents (29%) but methyldopa was replaced by beta-adrenocaptor blockers (17%), while the use of calcium channel antagonists (12%), ACE-inhibitors (7%) and low-dose Aspirin (4.5%), were found to have increased.

Several reasons such as poor blood pressure control (33%), side effects (26%), and poor compliance (19.3%) were responsible for the high incidence of prescription change (83%). Non-drug or general measures such as body weight reduction (diet and exercise) were rarely recommended (15%) whereas salt restriction was frequently recommended (88%).

Therefore, ABUTH Zaria management should provide adequate supply of first line drugs and increase the proportion of calcium antagonists and ACE - inhibitors in its pharmacy. Also, drugs used in the management of eclampsia and pre-

eclamptic toxaemia, (PET), should be provided in adequate amounts, since females predominate in the cardiac clinic and female hypertension was found to be pregnancy-related.

Restriction of Kolanut consumption (a source of caffeine which has pressor effect) and cessation of potash consumption (a rich source of potassium ions) should be recommended more to patients, as hyperkalemia is contra-indicated in any degree of renal impairment.

On the whole, it can be said that the therapeutic protocol of the cardiac clinic of ABUTH, Zaria conforms to WHO standards.

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CHAPTER ONE

1.0 BACKGROUND INFORMATION.

1.1 Introduction.

Hypertension or high blood pressure though not a disease entity, is a disturbance in the factors which control the level of systemic arterial pressure, due to primary defects or due to altered haemodynamics. [1]

The fundamental haemodynamic alteration is an increased resistance to the outflow of blood in parts of the systemic arteriolar bed. And according to Rose. [2] "..... hypertension is the level at which the benefits ..... of action exceed those of inaction. " In 1972, Sir G. Pickering,[3] in a search between normal and high blood pressure, argued that "there, is no dividing line. The relationship between areterial pressure and mortality is quantitative, the higher the pressure, the worse the prognosis. The World Health Organisation (WHO) expert committee on arterial hypertension,[4] has described hypertension as the persistent elevation of arterial blood pressure. In their report, the two critical features of high blood pressure were considered to be **elevation** and **persistence**. Elevated blood pressure which is persistent can be ascertained only by repeated measurements over a long period of observation. Also, blood pressure varies during the day and is usually considerably lower at night, both in normotensive and in hypertensive subjects. Therefore, a single, casual finding of elevated blood pressure does not justify the diagnosis of hypertension unless very high values are repeatedly found. So, at least three blood pressure readings should be taken on each of at least two different occasions before the subject is classify as hypertensive.

Although, there is no clear dividing line between normal blood pressure and hypertension, the WHO has simplified the definition based on consensus.[5] The WHO Experts have found that in any population, blood pressure values have a continuous bell-shaped distribution. So, it is not possible to

distinguish clearly" "pathological" [6] from normal values.

Indeed, blood pressure is a graded phenomenon, associated with graded risk factors. The higher the arterial pressure, systolic or diastolic, the greater the risk of complications, with involvement of both cerebral and coronary vasculatures.[7]

Diagnosis of hypertension alone does not necessarily indicate the need for drug treatment, according to WHO report of 1984[8], the current definition of hypertension, as given by the WHO experts committee on hypertension control [9] in 1996 "is a level of systolic blood pressure, SBP of 140mmHg or above, or a level of diastolic blood pressure, DBP, of 90mmHg or above. Normal blood pressure in adults over 18 years is equal to or below 140mmHg systollic and equal to or below 90mmHg diastolic while the pressure values between elevated and normal are known as borderline. [10]

But Since blood pressure is quite variable, the committee has advised repeated measurements over several weeks before labelling a subject hypertensive and deciding on initiation of treatment. The committee has further advised, confirmatory measurements over 3 - 6 months in mild or borderline hypertension, while, shorter periods are required in patients with more marked elevation of blood pressure or in those with complications. [11, 12]

These limits apply to adults of both sexes of any age. But the values for children that would be regarded as hypertensives are lower, but no precise figures have been generally accepted.

1.2 LITERATURE REVIEW.

1.2.1 Historical Background.

Normal blood pressure levels are maintained within narrow limits by a variety of homeostatic mechanisms of the carotid and aortic baroreceptor reflexes and by the control of sodium balance. [14]

Although emotional stimulation, exercise and over activity of the sympathetic nervous system, ("fear, fight and flight" response), cause a rise in blood pressure, this rise is small, reversible and appropriate to the physiologic requirements of the moment, (e.g. danger). But, persistent high blood pressure, HBP, is a very different situation. It involves a breakdown of the homeostatic pressure regulatory mechanisms of the body, which allows the arterial blood pressure to be continuously high. This condition often has serious consequences, on several organs such as the heart in particular (with the risk of heart attack); the brain, (risk of stroke), the kidney, (risk of kidney) failure and eye damage which may result in visual impairment or may even result in death. [15]

Hypertension is a condition which may show no symptoms hence tagged the "silent killer". Symptoms ascribed to it by patients such as headache, dizziness or drumming in the ears, are very rarely due to HBP [16]. Also, despite popular belief that headaches are a common symptom of HBP, controlled studies of unselected populations have shown that this is not the case[17] . This opinion exists because hospital and general practitioner studies are biased because a patient complaining of headache is more likely to have the blood pressure measured. Only one symptom has been shown to be more common among hypertensive subject s than among normotensive controls, and that is dyspnoea, probably due to a combination of a higher pulmonary venous pressure and left ventricular hypertensive disease. But patients with very high blood pressure (malignant

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hypertension), do suffer from severe headache. This type of headache is characteristic, it is worse in the mornings and may be present on waking. Such patients are few and there are many other causes of headache. Surprisingly though, studies of symptoms of **hypertension** show that people with HBP have less symptoms than normotensive controls.

Hypertension has been shown to be an important cause of death by the famous FRAMINGHAM HEART study, undertaken in Massachusetts, United States, from 1950 to 1989 [18], with 10,333 participants of ages between 45 and 74 year, and involving 51,756 examinations. The study showed that 37 per cent of men and 51 per cent of women who died of cardiovascular diseases had been previously noted to have HBP. The study involved the general population as well as hospitalised patients and those who consulted a doctor. Many of the deaths occur without warning [19] . A similar increase in risk has been calculated from life insurance data.

Death due to HBP may relate directly to very high blood pressures causing arteries to rupture[20]. Pressures greater than 180mmHg are found in very few people and such high pressures are associated with cerebral haemorrhage and heart failure due to increased work on the left ventricle. Even though such patients are few, they are important because these deaths are preventable by treatment. But majority of deaths from HBP are due to coronary artery disease, (CAD). This disease affects blood vessels which carry blood to the mayocardium. These deaths occur at less elevation of blood pressures (140 to 160mmHg SBP. But sadly, these deaths are not easily controlled by treatment of the hypertension [21]. There is currently great controversy about the evidence for and against drug treatment of mild hypertension with SBP 140 - 160mmHg and DBP 90 - 100mmHg. The general consensus about when to treat mild hypertension, is the presence of other risk factors such as cigarette - smoking, fat intake, overweight and

sedentary lifestyle [22] . The reason being that treatment of mildly raised blood pressure in patients without other risk factors for vascular disease, especially women, may produce side effects, and such side effects outweigh the rather marginal benefits of treatment.

There is no dividing line between normal and abnormal pressure. Therefore, in practice, "normal" values differ from group to group, whether young or old, pregnant or non - pregnant, etc. The actual level of blood pressure depends upon certain risk factors. Also, the actual measurement of blood pressure is affected by the defensive or alerting reaction of the subject to the examiner, resulting in incorrect reading of blood pressure. Therefore, measurements on several occasions allow subjects to familiarise with the examiner and the surroundings, free from stress and tension. It has been found in the general population that repeatedly measured blood pressure show "within subject" differences of up to 50 per cent that of" between subject" variations, in mean pressure levels, on separate occasions.

1.2.2 **Types Of Hypertension**.

A specific cause for a raised arterial pressure is found only in about 5 per cent of cases, even after thorough investigations [23] When no such cause can be found, hypertension is designated **essential** or **primary** , while the term **secondary** is used to classify those patients whose hypertension is due to such primary disorders as renal, endocrine and other disorders. Pressure values between elevated and normal are termed **borderline** hypertension. Such HBP may change and become severe. The elevation of pressure may be either progressive, benign hypertension or rapid i.e **malignant** hypertension. Pressure values may fluctuate, rise and fall and this is termed **labile** hypertension. Malignant hypertension if untreated causes death in the majority of affected patients within 6 to 12 months

because the rise in blood pressure is sudden and accelerated.

1.2.3 **Essential Hypertension**

This is the type without an identifiable cause. Therefore, only symptomatic treatment is possible [24]. And despite careful and energetic search for a primary cause, a diagnosis of essential HBP is made in 95 percent of hypertensive subjects i.e. diagnosis of exclusion [25]. This is the reason that many patients undergo minimal investigation usually urinalysis and blood urea and electrolyte estimation. (Table 1.1)

Table 1.1

First Line Investigation in Hypertension

Urine	Reagent strips for protein blood, sugar Microscopy for casts and cells culture.
Blood	Haemoglobin EST Urea, uric acid Creatinine fasting sugar, Electrolytes fasting lipids
Radiology	Chest X-ray
EGG	For left ventricular hypertrophy
Echocardiography	For left ventricular wall thickness.

---

30 Per cent of patient in the Fragmingham study with left ventricular hypertrophy in five years.

Experts argue that there is considerable doubt about the cost effectiveness of screening patients with HBP for a primary cause, since most of the investigations are highly risky, (such as IVP, intravenous pyelography which is uncomfortable for the patient and yields minimal therapeutic and diagnostic information). However, if the HBP either proves difficult to control with drugs or if there is sudden deterioration after prior good control or if the patient is below 40 years or if there is a suspicion of renal disease in the patient history or during clinical examination of the patient, then further investigations may be undertaken (Tables 1.2, 1.3).

Table 1.2

Features suggesting secondary hypertension during the clinical examination.

History	Examination
Known renal disease	Femoral pulses delayed
Thirst polyuria nocturia	Palpable kidney(s)
Dysuria	Enlarged bladder
Haematuria	Uraemic features
Loin pain colic	Oedema
Stones, gravel	Abdominal bruits
Abdominal Trauma	Feature of Cushing's or acromegaly
Analgesic consumption	Cafe au lait patches
Oral contraceptives	Neuronpromata
Other drugs (see table 4)	Orthostatic Hypotension.

Table 1.3

Feature suggesting need for further investigation.

Clinical features suggesting a primary cause

Abnorminalities of urea, creatinine, potassium in plasma

Proteinuria, haematuria, glycosuria

Hypertension under 30 years of age

Malignant hypertension

Uncontrolled hypertension.

The tendency to develop essential HBP is inherited due to the action of many genes i.e polygenic inheritance. But environmental factors also play an important role by contributing to the full expression of Hypertension. These environmental factors are therefore crucial in the search for possible preventive and non - drug treatment of this type of Hypertension.

Since nothing can be done to influence the genetic element. Factors that are important in development of essential hypertension were inferred from the study of communities with low level of blood pressure. Such communities were found to live in widely scattered geographical locations. They include various pacific Islands, mountainous and jungle areas of South America and various other locations in Africa[26] . But despite the ethnic diversity, these communities were found to share common features. These include their small and isolated communities, high level of physical activity combined with a low average energy intake, with clear periods of deficient food supply. Also, there was low salt intake, high potassium intake and their close interdependence. Each individual factor or a combination of several of these factors may be responsible for their low level of blood pressure. This led to the conclusion that environmental rather than genetic factors were important in the determination of blood pressure in these communities. Especially since people migrating from such areas to more complex societies generally show the usual rise in blood pressure with age. Such migrations were observed to involve the modification of several environmental factors simultaneously, even though it has not been easy to disentangle the respective influence of each individual factor. However, several aspects of these factors appear to be important in the development of essential Hypertension and they include body weight, sodium intake, alcoholic consumption, psycho -social factors, exercise and smoking amongst others [27] .

1.2.4 **Secondary Hypertension**

The cause of hypertension was identified by the WHO, in a community study using minimum laboratory tests, in 1.1 percent of cases [28]. But finding such a cause of HBP may spare the patient from a lifetime of taking drugs. And it is equally important that an underlying disease be discovered

which may require treatment. Such diseases include analgesic kidney damage, diabetes mellitus, obstructive uropathy, endocrine disease or collagen vascular disease [29]. Also clues may be found during clinical examination or in the patient's history (Table 1.3).

The extent of investigating the patient is based on the simple approach as outlined in table 1.1, while, further investigations is reserved for the patient in whom essential hypertension is unlikely or if the patient fails to respond to drug treatment or if the patient is non-compliant with his treatment, (Table 1.3).

A very common form of secondary hypertension is caused by ingestion of drugs and chemicals. (table 1.4).

This may be iatrogenic (prescribed drugs) such as hormonal contraceptives, corticosteroids or ingestion of drugs such as liquorice, cocaine, carbenoxolone, Amphetamines etc. Such elevation of blood pressure however **reverts** to normal when the substance causing it is no longer ingested. Therefore, HBP caused by drugs or exogenous chemicals, is easily preventable [30] . Other causes of secondary hypertension include renal insufficiency, endocrine disorders (e.g. diabetes) and organ abnormalities (e.g. liver failure). In addition, secondary hypertension may be pregnancy-induced and it may be associated with neurological disorders or it may be surgically induced i.e side-effect of surgery (Table 1.4).

Table 1.4

Causes of secondary hypertension

Unilateral renal Diseases	Bilateral renal diseases	Adrenal disorder	Drug associated	Other
Renal artery	Clomerulonephritides	Primary Aldosteronism	Oral Contraceptive	Coarctation of aorta
Stenosis	*Interstitial nephritis*	*Cushing's syndrome*		*Pre-eclampsia*
atheroma		Phacocmomocytom	Carbenoxolone sodium	Acute intermittent
fibrous dyspiasia		DOC excess		Porphyria
trauma		Corticosterore excess	Sympathomimetics	Acute lead poisoning
Pyclonephri is	Systemic Sclerosis	Congenital		CNS disorder
Obstructive nephr.	Other collagen vascular	Hyperplasi	inhibitors	raised intracranial
Vesico-ureteric reflux	disease	glucocorticod remediable	Application of skin	tension
Dysplasia		hypertension	mineralocorticoid	tetanus
Ask-Upmark kidney	thrombocytopenic	Ext. renin secreting	ointment	poliomyelitis
Trauma		tumours		Acromegaly
Tumour	Post partum renal failure	11β-hydroxysteroid		Alchohol addiction
(inluding renin secreting)	Haemolytic- uraemic	dehydrogenase		
Tuberclosis	Syndromes	deficiency		
Cyst	*Obstructive uropathy*			
Irradiation	Vesico-ureteric reflue			
	Dysplasia			
	Gout			
	Diabetes mellitus			
	Irradiation			
	Chronic renal failure			

Furthermore, **Oestrogen - progesterone oral contraceptives** (combination pill) rank first among the drugs with potential to cause HBP. Women taking 30 micrograms or more of oestrogen daily, record blood pressure increase for up to 2 years and then it remains level as long as the subject continues

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to ingest it. As reported by the WHO blood pressure reverts to normal in nearly all cases within 3 months of discontinuation of the contraceptive pill. The mean rise is about 15mmHg BP and 7-10mmHg DBP. In some subjects marked elevation which results in malignant hypertension may occur [31].

But contraceptive pills containing only progesterone do not cause HBP. Therefore, oral contraceptive should not be taken except the blood pressure is normal and it should be checked at least two times a year. If the blood pressure rises, an alternative contraceptive method should be prescribed because it is illogical and wrong to administer antihypertensives while the patient continues to take a pressor drug. **Liquorice** is often eaten in sweets and it is also used occasionally for treating peptic ulcer. It contains glycyrrhizinic acid which is a mineralocorticoid. Therefore, people who consume large quantities of liquorice may develop HBP associated with sodium retention and depletion of potassium. Also, **Carbenoxolone** contains glycyrrhizinic acid, the biochemical abnormalities and associated HBP following ingestion of liquorice or carbenoxolone also resolve following their withdrawal.

In a recent publication "perverse effects of an apparently harmless habit.....", a 47 year old woman with a long history of arterial hypertension was reported to have developed difficulty in control of blood pressure with associated hypokalemia. Thorough investigation showed low blood rennin and aldosterone and high urinary potassium. Exhaustive questioning later revealed that the patient regularly consumed non-negligible quantities of **liquorice** flavoured chewing - gum [32]. **Non-steroidal anti-inflammatory** agents, **NSAIDS** such as **indomethacin**, may cause HBP. Also nasal decongestants like **phenylpropanolamine** and other catecholamines such as ephedrine or **Amphetamine,** may cause transient elevation of blood

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pressure. Some **appetite - lowering** drugs (slimming pills) such as **fenfluramine** may have similar effect. In addition, intake of **foods** and drinks which contain large amounts of tyramine (cheese, beer, wine, chicken liver etc) can result in dangerous elevation of blood pressure if the subject is also taking **monoamine oxidase inhibitors** MAO - 1 such as **pargyline** [33]. **Coarctation of the aorta** is a congenital abnormality with narrowing of the aorta in which surgical correction is the appropriate treatment **Renal diseases** are of different forms and they may cause or aggravate HBP. These renal disorders may be caused by abuse of **analgesics, tuberculosis, benign** or **malignant tumours** etc. Other causes of secondary hypertension include **conn'ssyndrome, cushing'ssyndrome, intracranial tumours, phaechromocytoma, i.e** (tumour of the adrenal medulla), etc. These are rare. Elimination, withdrawal or treatment of these underlying disorders and known causes often lead to the prevention or cure of the hypertension [34].

1.3 Current Literature Relevant To The Research Questions

An interplay of genetic and environmental factors is the major cause of HBP. Most environmental factors act as risk factors or predictors of hypertension[35]. These factors are usually amenable to prevention or to non-drug treatment while the genetic factors cannot be modified. Factors which influence HBP include Age, Sex, height, weight, ethnicity, socio-economic status and geographical factors. [35] While the risk factors and predictors of HBP include genetic factors i.e. heredity and genetic background, family history (early life, childhood, the elderly, pregnancy) nutritional factors (i.e macro and micro- nutrients, vegetarian diet, polyunsaturated diets); alcohol, psychosocial factors, physical activity (i.e exercise and life style), environmental factors (i.e lead exposure, noise, environmental temperature) coffee and cigarette smoking. [35]

1.4 Personal Data Which Influence Hypertension

These include Age, Sex, Weight and Height (i.e Body Mass Index BMI), ethnicity, geographical location, nutritional factors and socio-economic status of the patient.

1.4.1 Age And Hypertension

Surveys and prospective studies consistently demonstrate a positive relationship between age and blood pressure in most populations, with diverse geographical, cultural and socio-economic characteristics[36]. Abrahams et,al [37], showed that blood pressure increased with age in both sexes in a study in ILORA town, Ibadan, Nigeria. A research in the United States on black teenagers showed that 30 per cent of healthy African - American teens were already showing elevated night-time blood pressure, [38] also in most western populations blood pressure is reported to rise with age. Females show very little rise in blood pressure till after menopause while males show a steady rise in blood pressure, and the WHO expert committee on control of hypertension [39] reports that in most western populations SBP tends to rise progressively throughout childhood, adolescence and adulthood, to attain an average value of 140mmltg by the seventh or eighth decade of life. While DBP rises at a slower rate with age, but the average value of DBP remains constant or declines after the fifth decade of life. Therefore, there is increased pulse pressure with age and isolated increase in SBP become more common with advancing age. The cause of this rise in arterial pressure with age is not clear, but it has been observed that unacculturated societies acquire a predisposition to age-related increase in blood pressure when they adopt a western lifestyle. This indicates an environmental influence such as the effect of change in diet. Also, plasma renin declines with age while catecholeamines rise with age. Probably, age-related rise in arterial pressure relates to structural thickening and degenerative changes in arteries and arterioles. But in some nomadic populations such as the nomads of Kenya or the natives of Papua

New Guinea, blood pressure does not necessarily rise with age [40]. Thus, there is reason to believe that age-related rise in blood pressure is neither inevitable nor a normal biological accompaniment of the ageing process. And according to Pickering [41], blood pressure tends to rise with age and differs in male and female. The rate in rise is not inherited but depends on environmental factors. Also, according to the WHO, there is no prospective therapeutic study of hypertensive children and adolescents, so epidemiological definitions are used. The **Report of the Second Task force on blood pressure control in children**[42] defined HBP in the young as average systolic and or diastolic blood pressure equal to or greater than the 95 percentile for age, on at least three occasions. (Table 1.5)

Table 1.5

Classification of hypertension in children and adolescents by age group [a]

Systolic and diastolic blood pressure (SBP and DBP), mmHg (kPa).

AGE	HIGH TO NORMAL[b]	SIGNIFICANT HYPERTENSION [c]	SEVERE HYPERTENSION[b]
7 days 8-30 days		SBP 96-105 (12.8-14.0) SBP 104-109 (13.9-145)	SBP ≥106 (14.1) SBP ≥ 110 (14.7)
≤ 2 years	SBP 104-111 (14.0-14.8) DBP 70-73 (9.33-9.73)	SBP 112 - 117 (14.9 - 15.6) DBP 74-81 (9.86 - 10.8)	SBP ≥118 (15.7) DBP ≥ 82 (10.9)
3-5 years	SBP 108 - 155 (14.4 - 15.3) DBP 70-75 (9.33 - 10.0)	SBP 116 - 123 (15.5 - 16.4) DBP 76-83 (10.1 - 11.1)	SBP ≥124 (16.5) DBP ≥ 84 (11.2)
6-9 years	SBP 114 - 121 (15.2 - 16.1) DBP 74-77 (9.86 - 10.3)	SBP 122 - 129 (16.3 - 17.2) DBP 78-85 (10.4 - 11.3)	SBP ≥130 (17.3) DBP ≥ 86 (11.5)
10-12 years	SBP 122 - 125 (16.3 - 16.6) DBP 78-81 (10.4 - 10.8)	SBP 126 - 133 (16.8 - 17.7) DBP 82-89 (10.9 - 11.9)	SBP ≥134 (17.9) DBP ≥ 90 (12.0)
13-15 years	SBP 130 - 135 (17.3 - 18.0) DBP 80-85 (10.7 - 11.3)	SBP 136 - 143 (18.1 - 19.05) DBP 86-91 (11.5 - 12.1)	SBP ≥144 (19.2) DBP ≥ 92 (12.3)
16-18 years	SBP 136 - 141 (18.1 - 18.8) DBP 84-91 (11.2 - 12.1)	SBP 142 - 149 (18.9 - 19.8) DBP 92-97 (12.3 - 12.9)	SBP ≥150 (20.0) DBP ≥ 98 (13.1)

1. Adapted from Task Force on Blood Pressure control in children (73); by permission of pediatrics, 79:1 1-25 copyright 1987. Note that adult classifications differ.
b. 90-94th percentile
c. 95 -99th percentile
d. > 99th percentile.

The prevalence of hypertension is at least one per cent in children and increases in adolescents, therefore blood pressure should be measured in children and adolescents especially where there is a family history of HBP because of the incidence of family clustering. Measurement is also justified because the higher the blood pressure and the younger the child, the greater the likelihood of secondary hypertension. In adolescents, use of alcohol, cocaine or other addictive substances should be considered as a possible cause of elevated blood pressure while for children, risk factors to be assessed include family history, obesity, diet, physical activity and anaemia. Laboratory tests for young patients are generally similar to those

recommended to adults, even though efforts should be made towards diagnosing secondary hypertension. The underlying cause, severity or complication of hypertension in children will determine the degree and types of intervention required such as drug therapy, weight reduction, lifestyle changes etc[43] . Hypertension is more frequent in people aged 65 years or older.

In absolute terms, hypertension is a greater risk factor of cardiovascular events in the elderly than in younger people. In developed countries, the 10 year risk of a major cardiovascular event was found to range from less than one per cent between 25 to 34 years; to greater than 30 per cent between 65 to 74 years. By the same token, antihypertensive therapy in the elderly was found to be highly beneficial.

1.4.2 Sex and Hypertension

Generally, it is known that women withstand HBP better than men, particularly before menopause. After menopause, the risk of death or morbidity is half that of men [44]. Early in life, there is little difference between the blood pressure of male and female, but from adolescence, men tend to have a higher average level. This has been observed in young and middle-aged adults [45]. In later life, the differences become smaller and the pattern may even be reserved. This trend results in a higher premature death rate in middle-age men with hypertension. In elderly females however, post-menopausal changes may account for the rise in blood pressure. And studies are in progress to evaluate the protective effects of oestrogen supplements, in old age.

In 1963, the University of Ibadan, in collaboration with the government of western Nigeria [46] embarked on a community study of hypertension, in Ibadan 1,969 males or 9.1 per cent had a blood pressure of 140/90mmltg

or greater. Similarly, 11.2 per cent out of 1,906 females had a blood pressure exceeding this level. With advancing years, percentage increases were recorded in each group. Also, the project found that from childhood up to 45 years, there was greater percentage of hypertensive males than females. But up to 60 years, the trend was reversed. And after 60 years and above, no clear pattern was reported.

1.4.3 Height and Weight and Obesity in Hypertension

Measurements of patient height (in metres) and weight (in kilograms), are useful in computing the Body Mass Index, BMI (body weight divided by the square of height). This BMI is useful in estimating obesity. Some experts [47] consider a cut-off of the 85 percentile for BMI as 27.8 for males and 27.3 for females aged 20 to 29 years. Other experts have accorded weights to the BMI, ranking BMI of 20-24.9 as a **good weight, 25 - 29.9** as over weight while BMI of 30 **and above** was rated as **obesity** [48] . There are simple and quick methods to check for obesity such as measurement of the waist, where, measurements above 88 centimetres suggest that the subject needs to lose weight. Even though excess weight may be either lean weight or fat tissue, BMI correlates well with the degree of adiposity. For instance, heavy muscled individuals would be considered obese using the BMI. But BMI assessment correlates well, with the risk of adverse effects on health and longevity. More precise assessment of obesity can be made with measurements of body density or with isotopic dilution methods, but these are unsuitable for routine use [49] .

The Framingham study demonstrated that 20 per cent excess over desirable weight clearly imparted a health risk. And a united states Institute of Health consensus panel on obesity agreed with this definition and concluded that a BMI above the 85 percentile for young adults constitutes

a health risk. The panel found the highest ratio among the poor and minority groups. But they noted that significant health risk at lower levels of obesity can occur in the presence of diabetes mellitus, hypertension, heart disease, or other associated risk factors. And from the United States Surgeon General comes the report that even mild obesity increased the risk for premature death, diabetes mellitus, hypertension atherosclerosis, gall bladder disease and certain types of cancer. And although overeating is the usual cause of obesity, environmental, cultural and genetic influences all contribute to obesity. Studies of biologic and adoptive siblings revealed a genetic influence on the amount and distribution of fat although the similarities were not as close in adopted siblings. Therefore, both nature and nurture contribute to obesity. In significantly obese patients, standard blood pressure cuffs result in erroneously high readings, because standard blood pressure curffs are too small for obese patients. Therefore, an oversize cuff should always be used. But a strong association has been observed even when accurate measurements are obtained. The mechanism by which obesity causes hypertension is uncertain but peripheral vascular resistance is usually normal while blood volume is increased. But thankfully, weight loss leads to reductions in systemic blood pressure independent of changes in sodium balance [50] . Additional studies from the United States have demonstrated strong associations between hypertension and obesity. DBP greater than 95mmHg and SBG greater than 160 mmHg or a report of current use of an antihypertensive drug was present in 6 i.e 32 per cent subjects out of a total of 19 subjects, in comparison with normotensive subjects , hypertensive subjects were of similar weight, but had greater central obesity (measurements of weight and hip circumference and cephalometry) [51]. Following weight loss, hypertension is observed to significantly decline. Thus conclusion was made that the obese subjects

most likely to have hypertension are male subjects or those with greater "central obesity", (central obesity is that increase in waist to hip ratio which correlates positively with hypertension, in many societies) [52] .

1.4.4 **Body Weight and Hypertension** .

There is a close relationship between blood pressure and body weight, both in children and adults, in developing and advanced societies. Those who gain more weight with advancing years show a more rapid rise in arterial pressure. Also, weight reduction has accompanied a fall in arterial pressure. In many studies strong associations have been demonstrated between hypertension and obesity (overweight) but following weight loss, blood pressure significantly declined. In particular, the accumulation of fat on the trunk or abdomen is closely related to HBP, as well as hyperlipidaemia and diabetes mellitus [53]

A new study from Boston [54] finds that extra weight and modest weight gains substantially increase women's risk of HBP. But for women who are already overweight, shedding pounds can help lower HBP. ..... However, weight reduction has been found to lower blood pressure in the majority of hypertensive patients, who were more than 10 per cent overweight. It was also beneficial on associated risk factors like lipid profile and insulin resistance [55]. And according to the WHO [56], there is a direct, strong and consistent relationship between weight and blood pressure. In most of the cross - sectional , prospective and observational studies reported, overweight was associated with a double to six fold increase in the risk of developing HBP. In western populations, 30 to 60 per cent of HBP has been attributed to obesity and from observational studies, each 10 kilogram increase in weight cause blood pressure rise of 2 - 3mmHg. But there is difficulty in measuring blood pressure accurately in the obese. And this may

account for the overestimation of arterial blood pressure with resultant better prognosis than would be expected otherwise [57] .

1.4.5 **Ethnicity and Hypertension**.

Population studies consistently show higher blood pressure in black communities than other ethnic groups [58], as reported by the World Health Organisation. This has been confirmed by recent reports from the United States that out of 50 million American plagued by HBP, the African - Americans are often prone to high blood pressure [59]. Other studies emphasize this ethnic variation in that black Americans of African origin have higher blood pressure levels than black Africans. This suggests that environmental augmentation of an ethnic predisposition may be responsible for the differences in their blood pressure values. But the role of ethnicity, independent environmental factors, needs to be clarified in other ethnic groups where countries show ethnic diversity in their populace. Ethnicity has also been found to affect age - related trends in HBP in black - Americans of African origin than in white Americans [60]. Average differences in blood pressure were shown to vary on these two groups from less than 5 mm Hg during the second decade to nearly 20mmHg in the sixth decade of life. Edward Frohlich has suggested that physiological differences associated with race and HBP may have important therapeutic implications. Areas of differences were reported to include the magnitude of total peripheral resistance; which differed in blacks and whites. Also, renal and cardiac haemodynamics involvement were more severe in black patients with essential hypertension [61].

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1.4.6 **Geographical and Altitudinal Location and Hypertension**.

As reported in studies by the WHO [62] , people living in mountainous regions of South America tend to have low blood pressure. However, these levels increased when the high altitude residents migrated to the less primitive low land regions. And this increase was associated with age. But in Ethiopia where highlanders have a higher socio-economic status than lowlanders the former had higher average blood pressures. Also the Tokelauans who migrated to New Zealand and Easter Islanders who migrated to Chile were found to develop a subsequent rise in blood pressure. But some small communities were found to have a tendency to develop higher than average blood pressure like the Hebridean Island of Tirée, where higher blood pressure have been observed than on the mainland of West Scotland. But many of these studies failed to disentangle the complicated and often conflicting influences of other factors including geographical and altitudinal locations on hypertension.

1.4.7 **Nutrition and Hypertension**

Consumption of a vegan diet (no milk, egg or meat) or a diet high in polyunsaturated fatty acids (fish liver oil, corn oil, Soya oil) is associated with lower blood pressure by about 5mmHg. But such diets are not acceptable to the generality of the population. This is probably because old habits do not die easily, in the general population [63]. The United State Council for Hypertension Research agrees that patients are tired of messages about healthy lifestyles changes. While doctors on their part are tired of delivering messages that are often ignored. Some specialists suggest that genetic research may help alert those at risk. Associate Professor of Medicine Dawn Wilson in her study of African-American teenagers [64] with elevated night time blood pressure, urged them to continue eating foods which they enjoy but to add potassium rich foods

which includes fruits, nuts, vegetable and yoghurt to their diets. For those who did she reported that their blood pressure dropped.

1.4.8 **Micronutrients**

Sodium Chloride

Of all nutrients that may modify arterial pressure, dietary intake of sodium chloride is most convincingly related to hypertension. In a significant percentage of hypertensive humans, the development of HBP is said to depend upon a high dietary intake of salt. This relationship of salt intake with blood pressure has been debated for decades. Robert Burton's 17th Century treatise[65] "the anatomy of melancholy", the author considers salt and salt meats to be great procurers of the disease. Writings on the evils of salt have older origins; the priests of ancient Egypt were said to have abstained from salt (so that their souls will be free from perturbation). Later, Dahl in 1961 proposed that individual responses to salt may be genetically determined because the vascular response to sodium which may itself be genetically determined could therefore be the factor which controls whether or not blood pressure will rise [66] . Although the practice of adding salt to food is an ancient one, there is little doubt that use of salt as a condiment only became widespread in modern times. Salt is required by man and estimates of normal daily requirements for adults is up to 15g per day. It is suggested that intakes of only 1 - 2g per day are more than sufficient for metabolic needs including periods of growth. But among societies or groups that habitually consume low salt diets, about 5g sodium chloride per person per day, or less, essential hypertension will be uncommon. While among societies or groups consuming high amounts of salt in excess of 10 to 15g per person per day, essential hypertension will be common. But individual susceptibility will determine which individual in a group will develop HBP [67]. In line with this, Kestlefoot in 1980 said

that "there is no essential hypertension on a no salt diet" [68]. Experimental and observational studies on excessive salt intake show direct relationship with development of hypertension. This relationship was shown to be more definite with increase in age. It has also been shown that a strong correlation exists between average salt intake and cardiovascular complications such as stroke, which are associated with hypertension. In Japan , the fish diet, containing much salt, has been associated with an above average incidence of high blood pressure. Also, primitive populations in Africa and Brazil, with a sodium intake less than 10mmol per day were found not to develop HBP, and their blood pressure did not rise with age. But since many other variables like body weight, nutrition, cultural factors as well as other dietary factors such as high food content of polyunsaturated fatty acids, tend to complicate the issues, as their low blood pressures cannot be attributable only to low salt consumption. In other studies by WHO [70] , observational data were analysed and regression slopes were calculated for SBP and DBP based on estimated daily sodium intake. In the 20 - 29 year olds, with daily salt intake of 100mmol of sodium, SBP of 4.9mmHg and DBP of 1.8 mmHg were recorded. While, those aged 60 - 69 years recorded 10.3 mmHg SBP and 2.9 mmHg DBP per 100 mmol of sodium per day. In another report based on WHO interpolation study, INTERSALT[71], 10,079 men and women in 52 centres, from 32 countries, projected that a 100mmol per day or lower intake of sodium over a lifetime could result in a 9mmHg rise in SBP from 25 to 55 years of age. But by age 55 years, this could cause a 16 per cent reduction in mortality per coronary heart disease, 23 per cent for stroke and 13 per cent death from all causes. And De Wardener [71a] postulated that a defect in renal excretion of sodium in hypertensive might account for the increase in a circulating natriuretic hormone or by its postulated effect on cation

transport in arteriolar smooth muscle. Also cation flux in red and white blood cells have been studied, as a complimentary study to the work of Wardener et al, and the result strongly suggest that subjects with essential hypertension have a genetically determined defect in cell membrane transport system. This defect was said to be responsible for increased intracellular sodium concentration. The same defect has however been also detected in normotensive relatives of hypertensive subjects. So, it has been suggested that this defect acting in concept with a high salt intake may eventually cause changes in cell physiology which could result in hypertension. And in Russia [72] tests of acute per oral salt loads were carried out in 73 persons aged 15 to 30 years. Results indicated the leading role of genetic influence in changes of the main parameters of the water - salt homeostasis in the formation of the pathological background of hypertensive disease, especially in its early stages in increased risk eg heredity risk, or in borderline hypertension. These results show an unstable regulation of the water - salt homeostasis with tendency to sodium retention or its increased excretion while in the advanced stages of severe hypertension, sodium retention is dominant. It is generally assumed that the effect of sodium chloride on blood pressure is specifically related to sodium. But in 1904, Ambard and Beaujard [72a] reported that both urinary chloride excretion and blood pressure were reduced in hypertensive patients consuming a salt - restricted diet. Based on a limited amount of information, it appears that high dietary intakes of both sodium and chloride are required to increase arterial pressure in man. But in patients with salt - sensitive hypertension, it was reported that dietary sodium chloride loading resulted in greater elevation of blood pressure than comparable sodium loading provided as bicarbonate [73]. The observation that the concomitant administration of both sodium and chloride is

required for development of salt - sensitive hypertension, provides a clue to the mechanism of salt - sensitivity. Increasing evidence suggests that HBP is related to greater plasma volume expansion with sodium chloride compared to the failure of selective dietary sodium loading to produce HBP, such as equimolar sodium citrate or sodium phosphate - loading. And in 1987 it was observed in man that [74] dietary sodium chloride loading resulted in both higher blood pressure and higher plasma volume than sodium citrate loading. These observations suggest that expansion of the extracellular fluid volume by dietary sodium chloride attributes to the pathogenesis of salt -sensitive hypertension. While the failure of selective sodium loading, without chloride, to increase blood pressure may be related to a re-distribution of sodium between the extracellular fluid and intra cellular spaces. The observation that dietary sodium bromide loading also elevates blood pressure, in contrast with non - chloride sodium salts, is consistent with this hypothesis because bromide transport is closely related to chloride transport [75].

Controversy regarding the role of sodium in human hypertension has developed because of the possible effects of other dietary constituent such as **potassium** or **calcium** which modulate the effect of sodium on blood pressure.

Furthermore, the fact that not all individuals exposed to a high sodium intake develop HBP strongly suggests a genetic or acquired impairment of the ability to metabolise a sodium load, and this may be involved in the blood pressure elevation effects of sodium. These observations and deductions gave rise to the hypothesis that human beings may be either **sodium - sensitive** or **sodium - resistant** [76]. Sodium - sensitive hypertensive individuals have been found to have significantly lower levels of plasma renin activity under basal as well as stimulated conditions than

sodium - resistant subjects [77]. Also, sodium - resistant subjects were found to have increased levels of catecholamines in plasma or urine than sodium - sensitive subjects [77a].

Opponents of the salt theory on the other hand maintained that within populations,. there is little or no evidence that the arterial pressure of the individual is closely correlated with sodium intake, or sodium excretion which is easier to measure. Studies of spouses with similar salt intake have not shown any striking influence of salt intake an arterial pressure. There have also been some epidemiological evidence from the Gothenburg study [78] of men aged 50 years; that there is a **weak negative** correlation between arterial pressure and sodium excretion. The same has been found in Scotland [78a] and the carefully organised study of the United States National Health and Nutrition Survey (NHANES) [78]. They both found no correlation between SBP and salt intake in a representative sample population. But there is no doubt that **extreme** dietary restriction of salt to less than (10mmol per day), thus reduce arterial pressure. But such extreme restriction would be quite unacceptable as a public health measure. The argument at present is whether a moderate reduction to a value less than 80mmol per day is worthwhile. It has also been argued however, that to be effective, sodium restriction should be applied in the crucial early months of life. Again, there is now some evidence of a small significant effect of such restriction on blood pressure [78]. But the possibility exists that sodium restriction at this age might carry hazards such as increased risk of severe hypovolaemia in the face of any stress caused by gastroenteritis, blood loss, or any other factor that acutely reduces extra cellular fluid, ecf value. Some well - controlled studies have shown a fall in arterial pressure with moderate sodium restriction [78]. Others have failed to do so [78]. Among subjects with mild hypertension or among children of

parents whose artenal pressure was known to be in the upper third of blood pressure distribution.

POTASSIUM. Some studies have suggested that increased intake of dietary potassium may lower arterial pressure but evidence is so far conflicting and the best designated investigations have not supported this speculation. Large international studies, INTERSALT, CARDIAC and others show an inverse relationship between blood pressure and dietary intake of potassium [79]. The INTERSALT study noted a decrease of 2.7mmHg in SBP for a 60mmol per day increase in the urinary excretion of potassium [79a,b]. On the whole, blood pressure has been more closely related to the ratio of urinary sodium to potassium than to either electrolyte alone. The INTERSALT analysis showed that a reduction of the 24 - hour urinary sodium to potassium ratio of 3:1 (70mmol of sodium per 55mmol of potassium) to 1:1 (70mmol of sodium per 70 mmol of potassium); which is associated with a 3.4mmHg reduction in SBP[80] .

MAGNESIUM. It has been shown to have protective effect on the cardio-vascular system [81a]. Some study shows that death rates from coronary artery disease and from sudden aarhythmias (without coronary occlusions) are higher in localities where water supplies are lacking in mineral contents [81 a,b,c,d]. It has been further documented that of all minerals in water supplies, magnesium seems to be the most important [81a]. Furthermore, the evidence though circumstantial, suggest that the increased magnesium content of hard water may provide sum protection against cardio-vascular disease. Animal studies have shown that restricted dietary intake of magnesium or potassium can be damaging to the heart. Dietary facts have reported to interfere with magnesium absorption [81e] and fat-rich diet may lead to negative magnesium balance, especially in persons subject to other magnesium – wasting influences. [81f]

Its depletion, whether due to diuretic therapy or otherwise may also provoke a rise in blood pressure which is reversible by magnesium supplements as suggested by a controversial study [81j]. Researchers have devised a diet that causes spontaneous mayocardial infaction in 75 per cent of test animals [81g]. Nutritionally, this diet is similar to diet of people in Affluent countries which contain high levels of fats, cholesterol, vitamin D, sodium, phosphate and protein but has lower levels of magnesium and potassium. The animals developed massive mayocardial infaction, atherosclerosis, hyperlipidaemia and high blood pressure. When magnesium of potassium intake was not restricted or when any other elements of the cardiopathic diets was normalised, cardiopathic changes were less severe. Studies indicate that magnesium influences blood pressure [81h-m]. The vasoactive role of magnesium is not completely understood [81 h]. but isolated iortic and coronary vessels have been shown to constrict when subjected to a low magnesium perfusate and to relax when exposed to a higher concentration perfusate [81 k,l]. Clinical studies show that HBP associated with magnesium depletion can be reduced to normotensive levels with magnesium replacement [81 k,l,m]. Observations by Whang Et el [81 n] in 1000 ambulatory hypertensive patients supports the view that hypomagnesaemie may aggravate hypertension [81b]. Hypomagnesaemic patients required more anti-hypertensive medication for blood pressure control than normomagnesaemics. This findings were recently confirmed that Dyckler and Wester [81 o]. who reported that a statistically significant decrease in systolic and diastolic blood pressure occurred in a group of ambulatory hypertensive patients following six months of magnesium supplementation. Calcium competes with magnesium for binding sites on the cell membrale. As serum magnesium falls, relatively more calcium, irons are able to enter the mayocardial cell,

lowering its excitability threshold. This can induce vasoconstriction, leading to the occlusion of previously patent but arteriosclerotic blood vessels [81 b,o]. According to WHO, several population surveys and intervention studies have not found a major independent role for such micro - nutrients as magnesium, zinc and calcium, in the determination of the risk of future development of high blood pressure. [81]

CALCIUM. Mc Carron et al [82] postulated that abnormalities of calcium metabolism are involved in the pathogenesis of essential hypertension. The NHANES - 1 survey also showed a striking correlation between low dietary calcium - intake and high SBP. Also, low dietary calcium appeared to be the most consistent dietary predictor of hypertension. They calculated that a person consuming less than 300mg per day of calcium had an 11 - 14 per cent risk of hypertension. Also, a diet containing 1200mg per day had an associated risk of 3 - 6 per cent [82]. There may be important interactions between calcium and other dietary constituents so that the relationship and mechanism may not be simple. There is now an evidence for an abnormality of calcium metabolism either within cells or across their membranes. Support for this comes from studies of Robinson et al in London [82]. They found that the forearm vascular resistance of hypertensive subjects was reduced more by the calcium channel blocking agent VERAPAMIL when it was infused into the brachial artery; than by NITROPRUSSIDE infusion. And the reverse was found in normotensive subjects. This suggests a functional difference in the role of calcium in the control of arterial smooth muscle tone in hypertension.

1.4.9 **Macronutrients and Hypertension**.

There is gathering evidence for a causal relationship between macronutrients, (fat, fatty acids, carbohydrates, fibres and protein), as suggested by observational studies, with blood pressure (excessive intake of carbohydrate and fat causes obesity). Also, there is some evidence that short - term diets containing macronutrients affect blood pressure in normotensive or in mild hypertensive. [68]

1.4.10 **Socioeconomic Status and Hypertension**.

There is inverse relationship between socio-economic status and HBP. In the socioeconomic groups of advanced countries, consistently higher levels of blood pressure and a higher prevalence of hypertension have been noted [83] This relationship is also true with levels of education, income and occupation, according to experts. But in developing countries and societies higher levels of blood pressure and a higher prevalence of HBP have been noted in upper socioeconomic groups. This is true in the initial stage of cardiovascular disease epidermiology, also experience in most societies has shown that the social groups affected are reversed as the epidemic advances [84].

1.4.11 **Occupation and Hypertension**.

Researchers in France conducted a prospective transversal study on more than 4,000 individuals including almost 800 women working in the same company with a view to comparing the prevalence of a certain number of classical cardiovascular risk factors in two types of populations, the service and manufacturing workers, in Paris. And also to understand these workers better so as to develop educational and information campaign, specifically adopted to their needs. Several elements were recorded during physical examination (including blood pressure, blood cholesterol, smoking history,

blood triglycerides, blood sugar, physical activity). A level above a determined threshold was considered as a risk factor. For men in service industries, the percentage of heavy smokers (24%), hypercholesterolaemia (18%) and hyperglycaemia (7%) were significantly higher than in the manufacturing sector (19.3%, 15% and 2.4%, respectively).

In the manufacturing sector, the percentage of men with HBP (15%), hyperglyceridemia (10%), who were overweight (24%), or had a low high density lipoprotein level HDL (10%) were significantly higher than in the service sector (3.1%, 7.5%, 20% or 8.2%, respectively). The percentage of women smoking more than 20gramme of tobacco per day 25.5%) in the service sector was significantly higher than that in manufacturing industries (4.25%). But in contrast, percentages from the manufacturing sector the percentage of hypertensive (6%) and obese (24%) women were significantly higher than those in the service industries (1.1%, and 16%, respectively). This study was designated the CESAME survey by occupational health physicians in France [85] .

1.5 FAMILY HISTORY THAT PREDICTS HYPERTENSION.

A family history of raised blood pressure is common and it is one of the strongest risk factors for future development of HBP in an individual [86]. Population studies have shown greater correlation of blood pressure between siblings than between parents and offspring's [86]. Twins have been shown to have greater association than spouses - this suggests that genetic factors are more important than the environment [87]. Population studies also show that close relatives of a subject whose blood pressure is 50mmgHg above the population average, will have blood pressures 14mmHg above the average value. According to the WHO, the blood pressure of first -order relatives (ie parents and siblings), of the same age and sex is additive at all levels of the blood pressure. There is evidence that blood pressure

trends of an individual are determined very soon after birth [88]. And long term studies of adult relatives of hypertensives have shown that individuals retain the level of their blood pressure relative to others. This phenomenon called "tracking" [89] can be followed from early childhood. Although studies of blood pressures of infants do not show strong correlation's with pressures taken a few years later, longitudinal studies of arterial pressure have shown that older subjects in the top or bottom10 per cent of their group, in respect of arterial pressure, stay in the same percentile for many years. Those whose pressure is at the upper end of the range as young adults may be destined to be the hypertensives of the future. There is much debate and few facts about the reasons for this finding. However, some recent surveys show that height and body weight are important predictors of blood pressure and involve skeletal age and growth hormone levels. But nevertheless, such "tracking" from childhood only accounts for about 30 to 50 per cent of the variation in adult blood pressure. In general, early presence of high pressure have not been very predictive of future risk. Arguments continue about the relative importance of genetic influence and those of the common family environment, such as diet and salt intake. The TECUMSEHT study [90 a,b] reported by the WHO was based on a group of 40 year - old people with HBP. The results showed that they had higher than normal blood pressure at the age of 7 years. But the success rate of "tracking" to predict adult blood pressure in children is limited even though it is effective in predicting group blood pressures.

1.5.1 **Genetic Factors and Hypertension**.

The relationship between HBP and genetics has been thoroughly researched. Initially, Platt [91] proposed a single dominant gene based on his study of the blood pressure of relatives of hypertensive patients. This

hypothesis was later refuted and currently, HBP is regarded as polygenic in aetiology. Pickering later proposed a multiple genetic influence on HBP which is yet to be negated. A large number of genes are being studied especially the angiotensin-II converting enzyme, (ACE - II) and angiotensinogen gene polymorphism [92] . Molecular genetics may enhance our ability to give special attention to some susceptible individuals. Many phenotypic characteristics have been investigated in both normotensives and hypertensives, with a family history and those without family history of HBP. These include sodium - potassium co-transport and lithium - potassium co-transport. Also, blood pressure response to salt load, exercise, exposure to cold, mental stress and plasma or urinary levels of various hormones, catecholamines and renin. Several of those showed a positive relationship with a family history of HBP, but are not considered as causes of HBP. However, genetic research may help alert those at risk to pay attention. There is new research from the United States, that a mutated gene can double the risk of stroke. If supported by further studies this discovery could lead to new treatments and ultimately help to avert strokes [93] . But it has long been recognised that blood pressure elevation may be an inherited trait. Reports indicate familial similarities of blood pressure levels [94,a]. A unique models for analysis of genetics and environmental factors has been the **study of families of monozygotic (identical) twins**, that marry unrelated spouses. The relationship between the non - twin spouses is that of genetically unrelated individuals. While the children of identical twins i.e. genetically identical, are genetic half siblings, since they share approximately 50 per cent of their genes. Also, the quantification of the genetic influence on blood pressure has been from the **study of identical twins adopted *into separate environments* after birth** [95] . These studies provided information which indicated that 60 per cent of SBP

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and DBP level can be due to genetic contribution. The rest being from environmental factors, and or acquired abnormalities which affects blood pressure.

1.5.2 **Early Life and Hypertension**.

Recent studies suggest that an adverse environment during critical periods of development in fetal life and infancy, predispose an individual to risk factors for HBP and other cardiovascular disorders. Longitudinal studies of children and adults showed that low birth - weight is inversely associated with high blood pressure. This resulted in the hypothesis of "fetal programming." But migration studies gave evidence that blood pressure patterns are strongly influenced by the environment of the host country [62]. This such programming is not the only factor influencing adult blood pressure.

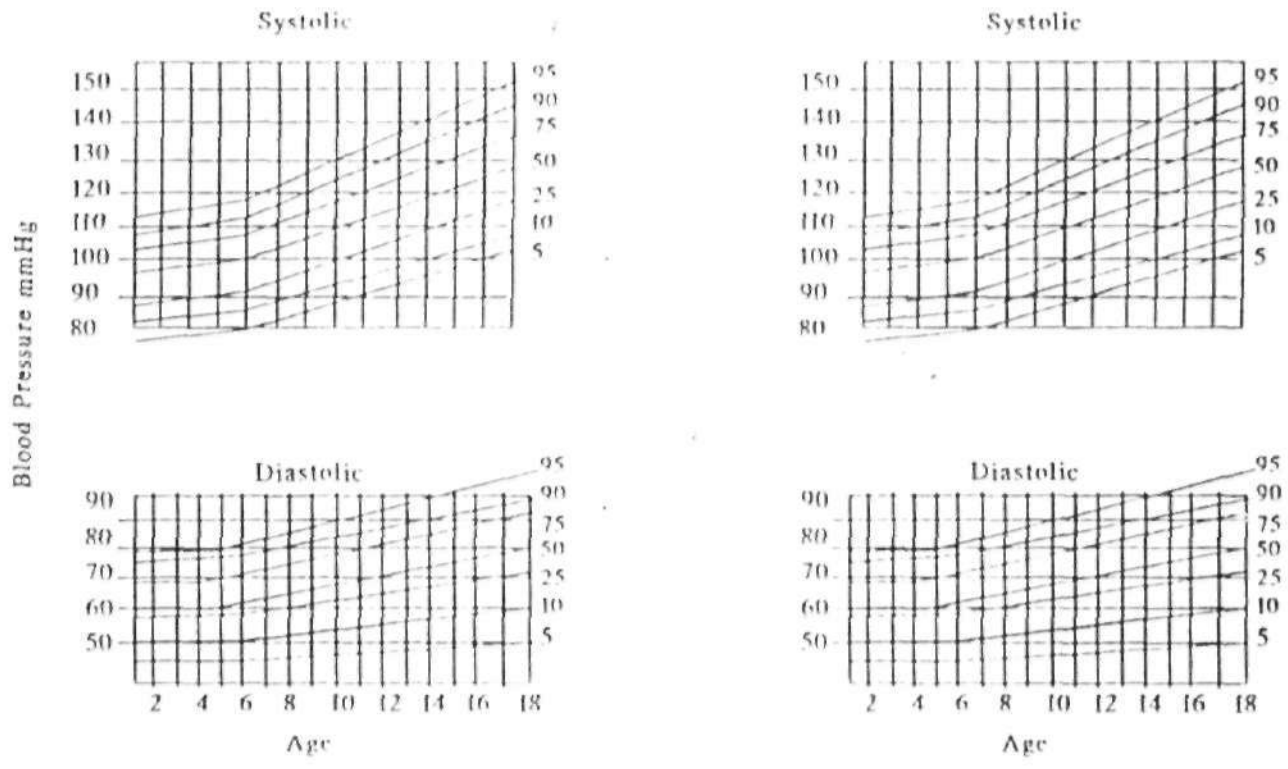
1.5.3 **Childhood and Hypertension**.

Blood pressure in children depends on age even more than in adults. The distribution of pressure in similar boys and girls and in both sexes show a steep rise in SBP and to a lesser extent in DBP, between the ages of 5 to 15 years. This rise correlates well with sexual maturation. Also, **children that gain weight rapidly are more likely to have a rapid rise in blood pressure as they grow up** [97]. Thus, when evaluating the blood pressure of a child, body size as well as age are important considerations. In children as it is in adults, blood pressure should be measured in quiet surroundings in the absence of exciting or alarming stimuli and in a reassuring and friendly environment. The definition of HBP in childhood is as arbitrary as in the adult. But unlike in adults, little is known about how the long term prognosis correlates with blood pressure levels. Thus, it is difficult to delineate blood pressure in childhood. But pressures above the 95 percentile require special attention (Fig 1.1).

Figure 1.1

Hypertension in Special Groups

Percentiles of blood pressure (right arm, seated) in boys (left) and girls (right).



* Source Report of the Force on Blood Press Control in Children. Padiatrics 59(Suppl.):803(19

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Also it is likely that children whose blood pressure is relatively high are those who are likely to develop HBP in adult life. Apart from drug - induced hypertension, most forms of secondary hypertension are seen in childhood. The first cause to look for in a child with HBP therefore, is coarctation of the aorta, even though renal, adrenocortical and adrenomedullary forms of HBP can also occur, especially those due to inborn errors of corticosterod biosynthesis as well as the rare renin secreting tumour, all of which can be detected in early life. But primary or essential HBP predominate in childhood. In similarity to adults, HBP in children is usually without symptoms or sign. Therefore, blood pressure should be measured whenever a child is being examined by the family doctor or even at school. Such routine checks, as suggested by the WHO, provide valuable information and the child gets used to blood pressure measurements which lowers the risk of **inducing neurosis**. But some alerting signs to the possibility of HBP in a child include failure to maintain normal growth curve, and on the return of bed - wetting (enuresis) should be a good reason for blood pressure measurement.

1.5.4 **Other Predictors of Hypertension in Children**.

Echocardiography is being used to study the response of blood pressure in children to exercise and to weight - gain. Also the relationship between blood pressure and left ventricular mass which is also determined by echocardiography [98], retinal examination, urine analysis, hormonal levels etc.

1.5.5 **Blood Pressure in the Elderly**.

The elderly have been arbitrarily defined as the section of population aged 70years [99] and above. Among this group, elevated blood pressure is the

major factor associated with reduced life expectancy quite apart from age and sex. But the minimum number of laboratory and investigative tests should be carried out in the elderly because of the risk and small diagnostic yield of such procedures. Hypertension is considered a much greater risk factor for cardiovascular events such as stroke, in the elderly than in the young people. In developed countries the 10 year risk of major cardivascular event, according to the WHO [100] , ranges from less than 1 percent (ages 24 to 30 years) to over 30 percent in those aged 65 to 74 years.

1.5.6 **Pregnancy and Hypertension**

The arbitrary limit of 140/90mmltg has been associated with hypertension in pregnancy [101]. This is because after the first 3 months, or trimester, of pregnancy, blood pressure becomes lower than pre-pregnancy levels due to peripheral vasodilatation, especially in the young and fit pregnant women. This pressure level may be even lower for certain ethnic groups, according to the WHO [101] The Hypertension of pregnancy is also called **toxaemia of pregnancy, pre-eclampsia, eclampsia, hypertension gestosis or pregnancy - induced** as well as **pregnancy - associated hypertension** [102] It is the major cause of premature birth and perinatal death, and is also responsible for 20 to 33 percent of all maternal deaths, usually due to cerebral haemorrhage, as reported by the WHO [101]. In developing countries, hypertension in pregnancy is a major health problem [101]. Infants of mothers who have Hypertension with proteinuria in late pregnancy are small and often stillborn [102]. Such infants, have a high risk of dying in the neonatal period. But the incidence of this disease varies widely, according to reports. Most of the information were obtained from hospital studies. so they are not representative of the total population. But a reasonable estimation, according to the WHO is that less than 5 percent of pregnancies are complicated by blood pressure elevation.

1.5.7 **Pregnancy - Induced Hypertension (PIH)**

Hypertension arising in pregnancy is described as the presence of a normal blood pressure before 20 weeks of gestation [103]. Hypertension in pregnancy is defined by experts as a rise in SBP of at least 140mmhg or a DBP of 90mmhg. And as the incidence of protenuria increases with the diastolic pressure (DBP), once the DBP exceeds 115mmhg, 35 percent of women exhibit proteinuria and this signifies both maternal and fetal danger.

Pregnancy - induced hypertension, PIH may develop during pregnancy, labour or in the puerperium , in a previously normotensive, non - proteinuric woman[104] . It may be any of these types. Firstly, **Gestational hypertension without proteinuria** which may develop during pregnancy (antenatal) for the first time during labour or for the first time in the puerperium. Secondly, **Gestational proteinuric hypertension** which may develop during pregnancy (antenatal) for the first time in labour or for the firs time in the puerperium. And thirdly, **Gestational proteinuria without hypertension**, (Pre-eclampsia) this develops during pregnancy (antenatal), for the first time in labour for the first time in the puerperium. The peripheral problems of PIH include prematurity, Intra-uterine asphyxia, failure of intra-uterine growth often due to placental ischaemia and infarction caused by obstructive lesions and in the uterine spiral arteries PIH is common in primigravidae, (woman's first pregnancy), especially in old primigravidae, ("old mothers"). In general, it seems likely according to experts that PIH is about 15 percent in Western European countries where approximately 10 percent of this population develop proteinuria [104]. The variation in incidence of PIH may be due to other conditions such as multiple pregnancy, diabetes mellitus, severe rhesus iso-immunisation and

hydramnious, which increase the incidence of PIH. A 50-year study of **the daughters, daughters-in-law, sisters and grand -daughters of women who had PIH** suggested that severe pre-eclampsia, is inherited as a **simple autosomal recessive gene.** But because of changing incidence of PIH in many countries, the variations in relation to race and climate; it is assumed that any genetic factor acts as a predisposing factor and not a final determinant. The causes of PIH have been broadly classified into triggering factors such as vasoactive substances (renin-angiotensin-aldosterone system RAAS, kallikreins, (Bradykinins) eicosanoids (i.e prostaglandins, thromboxane, and the other metabolites of arachidonic acid), haematological changes and the immune system. In the United States, the incidence of pre-eclampsia has been reported as ranging from 2.5 percent to 7 percent [104]. And the risk factors for its development were young maternal age, previous pre-eclampsia, twin pregnancy, chronic hypertension, diabetes mellitus and hydatidiform molc. Vasospasm was also considered central to the pathologic changes of pre-eclampsia, by these workers. They also suggested that its trigger was an imbalance between prostacyclin, (prostagladin (12)), and thromboxane. The types were said to range from mild to severe forms and eclampsia which occurs with severe disease. The workers reported that preventive strategies such as calcium supplementation and low-dose aspirin were being investigated [105] .

1.5.8 **Pregnancy - Aggravated Hypertension, PAH**

This has been described as HBP with or without proteinuria which occurs during pregnancy, in a woman with chronic hypertension or chronic renal disease. It may be diagnosed either before or during or persisting after pregnancy. It is of various types. There is **chronic hypertension without proteinuria, chronic renal disease (i.e. proteinuria and hypertension)**

as well as chronic **hypertension** with **superimposed pre-eclampsia,** (i.e. proteinuria developing for the first time during pregnancy in a known hypertensive woman) [106]. However, chronic hypertension which precedes and continues through pregnancy is rare and affects 3 percent of pregnant women according to reports from the WHO [106]. This is significant because it correlates well with about five - fold increase in the risk of developing pre-eclampsia. And this is the reason for the higher perinatal mortality observed in chronically hypertensive women. But if such women do not develop pre-eclampsia, then they usually can expect a normal pregnancy.

1.5.9 **Unclassified HBP With or Without Proteinuria**

This type of hypertension is associated either with or without proteinuria. It is found either at first "booking" examination after the first 20 weeks of pregnancy (140 days) in a woman without known chronic hypertension or without chronic renal disease. Or it may be found during pregnancy, labour or the puerperium where information is insufficient to permit classification. This type of PAH include **unclassified hypertension without proteinuria unclassified proteinuria without hypertension** as well as **unclassified proteinuric hypertension** i.e. **pre-eclampsia.**

1.5.10 **Eclampsia**

This can be described as one complication of the hypertensive disorders of pregnancy. It is the convulsive phase of pre-eclampsia called "eclamptic fits". Eclamptic fits are associated with haemorrhage; and are described as the terminal cerebral pathology of the sudden increase in arterial pressure characteristic of pre-eclampsia [107].

1.5.11 **Oedema in Eclampsia**

The international society for the study of HBP in pregnancy, ISSHP recently recommended exclusion of oedema from the diagnostic classification of pre-eclamptic toxaemia, (PET) [108]. This is because oedema or features of excessive weight-gain though common in pre-eclampsia does not enhance its diagnosis because oedema occurs in up to 70 percent of normal pregnancies.

1.6 SOCIAL HISTORY AND RISK FACTORS FOR HYPERTENSION

Risk factors for HBP include intake of alcohol, cigarettes and coffee, where as environmental factors are exemplified by physical activity and psychosocial factors.

Risk factors do not cause HBP by themselves but they contribute to the neurohumoral, metabolic and haemodynamic mechanisms that interact to regulate basal blood pressure level as well as respond to stimuli [109]. A change in their interplay cause a change in blood pressure. Aberrations in these mechanisms can be identified but risk factors are difficult to elucidate because several criteria must be evaluated. These include the strength and consistency of association, the cause must precede the effect, dose-response relationship, compatibility with current biological knowledge, epidemiological validity irrespective of confounding factors and experimental evidence in humans. Some of these criteria are met by observational studies of prospective cohorts and by intervention trials, which provide major epidemiological evidence. And survey of time trends generate hypothesis or provide supplementary evidence. Cause and effect cannot be established in known hypertensive just as a search for risk factors in people with established high blood pressure, would be too late in the natural course of the condition.

1.6.1 **Alcohol and Hypertension**

The general effect of alcohol is vasoconstriction even though it causes skin vasodilatation. It is now known that even moderate alcohol intake raises blood pressure, because of vasoconstriction especially in muscle bed vasculatures. In one important study, the well know fall in blood pressure on admission to hospital was shown to result at least in part from alcohol withdrawal [110]. But when patients supplemented the hospital diet with 3 pints of beer per day (1.5litres), blood pressure did not fall. Several population studies have shown a strong positive correlation between chronic alcohol intake and blood pressure. This relation is independent of any concomitant weight-gain. When patients remain hypertensive despite drug therapy one should endeavour to discover whether there is a hidden alcohol problem. It has been estimated that a 1mmHg fall in blood pressure results from 10ml reduction in ethanol per week.

Alcohol consumption has been consistently related to high blood pressure in cross-sectional as well as prospective observational studies in several populations, according to the WHO [112]. The WHO has noted that both acute and chronic effects of alcohol intake are independent of obesity, smoking, physical activity, sex and age [111]. But it was not clear if a threshold effect exists. When two or more drinks are consumed per day, SBP was found to rise about 1mmHg and DBP about 0.5mmHg per alcoholic drink. Daily drinkers were observed to have SBP and DBP levels respectively of 6.6 mmHg and 4.7mmHg higher than once- a week drinkers, which was independent of the total weekly quantity [112].

1.6.2 **Cigarette Smoking and Hypertension**

Cigarette smoking causes a short term rise in blood pressure. Long term effects of cigarette - smoking in, most studies show a lower blood pressure in smokers, but it appears to be related, to a large extent to body weight. And malignant hypertension is more common in cigarette smokers than non-smokers. Their cigarette - smoking should be considered when measuring blood pressure.

1.6.3 **Caffeine and Hypertension**

Drinking coffee (200mg caffeine) elevates blood pressure by about 10/8mmHg for 1 to 2 hours. In Nigerians a more common source of caffeine, especially in the low socio-economic class is Kolanut. It is important to consider Kolanut intake when measuring blood pressure.

1.6.4 **Patient Environment and Hypertension**

These environmental factors include, lead exposure, environmental temperature, noise and stress.

1.6.4.1 **Environmental Lead Exposure**

The second nutrition survey of 20,322 persons (NHANES - II), found a direct relationship between lead blood levels and both systolic and diastolic blood pressures, particularly in young men and women (21 - 55 years) [114]. The possible reason was thought to be that the pressure effect of lead operate via a lower serum calcium, since both ions follow a similar metabolic pathway. However, the researchers advised caution about predictions of the public health implication which the results could have, through the petrol engine. Although this explanation could also provide the reason for the difference between urban and rural blood pressures, the regression coefficient of the NHANES-II study was low, meaning that blood lead levels

might only account for a very small proportion of the blood pressure variability in the population. Furthermore, studies in the United Kingdom do not confirm an association between blood lead concentration and blood pressure. In addition, studies of workers in industries with great exposure to Lead show no high prevalence of HBP related to blood Lead levels.

1.6.4.2 **Environmental Temperature**

The Medical Research Council trial (MRC) of 17,000 subjects with mild HBP revealed that for temperature difference of about 20°c between summer and winter, there is a difference of 3mmHg on blood pressure from the young and 7mmHg for older subjects, in the united kingdom.

1.6.4.3 **Environmental Pollution**

NOISE: Studies of noisy environments such as airports communities or heavy industries have shown that raised environmental noise levels can raise blood pressure (enhancement of sympathetic nervous system drive leading to defuse vasoconstriction resulting in increased systolic blood pressure).

Air and **Water** pollution have been reported by the WHO to be implicated as risk factors for high blood pressure [114]. But they concede that more research is needed on this even though the public should be protected from pollution because it affects health in many other ways besides contributing to HBP.

1.6.4.4 **Physical Activity and Hypertension**

Sedentary and unfit normotensive individuals have been reported to have a 20 - 50% increased risk of developing HBP during follow - up when compared with their more active and fit peers [115] .

1.6.4.5 **Psychosocial Factors and Hypertension**

There is evidence that various forms of acute mental stress increase blood pressure, even though WHO experts have little evidence that long term stress has long-term effects [116 a], when divorced from confounding factors such as dietary habits and socioeconomic factors, as such they suggest further research in order to establish causality or permit quantification of the risk. Other studies however have found that people exposed to repeated psychogenic stress may develop hypertension more readily than otherwise similar people not so stressed. For instance, air traffic controllers, who work under tremendous psychological stress, annually develop hypertension at a frequency 5.6 times greater than do non professional pilots who were initially comparable in physical characteristics. Also, men repeatedly stressed by high levels of noise were found to have significantly higher blood pressures and more hypertension [116 b], than the control group. And in another study, nuns appear to have lower blood pressures than women working outside a sheltered environment [117]. Also, in at least 22 instances, populations living in small, cohesive, protected societies have been found to have low blood pressures which do not rise with the ageing process. Those who abandon such an environment and migrate to more urbanised, modern, disorganised societies have higher blood pressures which rise with ageing [118]. Even though it is obvious that other environmental factors may be responsible but in some of these groups the relationship between hypertension and social disorganisation seems strong. Other studies have found various personality traits among people (such as a tendency to suppress emotions [119], free-floating and phobic-anxiety and depression) to be more prevalent in hypertensives [120] . However, the casual connection has been questioned and [121] no correlation was found

between depression and hypertension [122]. Also the higher prevalence of HBP among blacks has been related to their higher level of discontent and other social stresses [123]. But the Negroid race may not be peculiar in this regard [124]. **Caucacians in** the lower class and with less formal education also have more hypertension. [125]

A similar study was carried in Poland involving 14 male patients with mild hypertension, aged 20 - 46 years (mean 32.4 years) who had their arterial blood pressure monitored by measuring it three times daily for 6 weeks. Prior to and after the study period, psychological tests were carried out using (Gough's test and Spielbergers questionnaire). All patients also underwent Krae Plins test under stress conditions two times during the study. Their results indicated that there is significant correlation of personality response syndromes (such as) need for acceptance, inferiority complex, need for success, trust in themselves, and anger) and some values of blood pressure. These findings strongly suggest that the personality syndrome is related to HBP.[126]

1.7 CLINICAL HISTORY AND HYPERTENSION

This includes age at diagnosis, presenting complaints and incidence of co-existing illness or illnesses.

1.7.1 Age at Diagnosis of Hypertension

Hypertension is one of the risk factors for cardiovascular diseases. The absolute risk can be modified by one or more of several risk factors. The modifiable factors include raised systolic and diastolic blood pressures, smoking, left ventricular hypertrophy, diabetes, renal diseases, micro-albuminuria, obesity and sedentary life style. While those not modifiable include age, sex, family history of premature, cardiovascular disease,

previous cardiovascular events (e.g. heart attacks) and previous cerebrovascular events (e.g. cerebrol-vascular accident) [127] . And According to Robertson and Ball [128] . It is now known that children who gain weight most rapidly, especially in their teens, generally show the most rapid age - related rise in blood pressure and are also likely to have higher blood pressure in adulthood. The absolute risk may vary widely among individuals depending on the age at which they develop hypertension. The elderly, according to studies will suffer further serious events each year with a risk of 3 - 5 in 100 [129 a, b] while, young patients, with no other risk factors, will suffer a serious event each year a risk of 1 in 1000 [130] . And although treatment or hypertension will reduce risk in both categories of patients, clinical benefits may take some decades to become apparent in young patients at low initial risk.

1.7.2 **Co-existing Illness Presenting Complaints: Consequences of Organ Damage in Hypertension**

Three organs show particular susceptibility to raised blood pressure with obvious consequences on their vasculatures. These organs include the brain, eye and kidney, manifest important pathological changes due to the effect of hypertensive disease[131] as outlined in Tables 1.6 and 1.7.

Table 1.6: Frequency of various diagnoses in hypertension patients

Dignosis	Percentage of Group
Essential	90
Oral contraceptive induced	4
Renovascular disease	3
Chronic renal disease	2
Primary aldosteronism	10.4

From Ferguson (1975) Ann intem Med. 82, 761-756, by permission.

Table 1.7

A. Risk factors

- Family history of hypertension and cardiovascular disease
- Family and personal history of hyperlipidaemia
- Family and personal history of diabestes mellitus
- Smoking habits
- Obesity: amount of physical exercise.
- Personality of the patient; social environment.

B. Symptoms suggesting secondary hypertension.

- Family history of renal disease (polycystic kidney)
- Renal disease, urinary tract infection, haematuria, analgesic abuse (parenchymal renal disease)
- Oral contraceptives, liquorice, carbenoxolone, nasal drops (hypertension due to drugs)
- Episodes of sweating, headache, anxiety(phaechromocytoma).
- Episodes of muscle weakness and tetany (hyperaldosteronism).

C. Symptoms of organ damage

- **Brain and eyes: headache, vertigo, impaired vision, transient ischaemic attacks, sensory or motor deficit.**
- **Heart: palpitations, chest pain, shortness of breath, ankle - swelling.**
- **Kidney: thirst, polyuria, nocturia, haematuria.**
- **Pewripheral arteries: cold extramities, intermittent, claudication.**

1.7.2.1 **The Brain**

The pathological changes in the brain due to HBP include stroke or cerebrol-vascular accident (CVAs), Transient ischaemic attacks, (TIAs), subarachnoid haemorrhage and dementia. **Dementia**, also called vascular dementia is a common sequel to HBP in populations of many countries, even where other risk factors (such as high levels of blood lipids) seems to be less common. [132]) even though the exact association , between dementia and hypertension is still largely obscure. On the other hand, multi-infarct dementia, with progressive deterioration of mental function accompanied by focal neurological signs, is usually associated with HBP and patients could benefit from antihypertension treatment [132]

stroke. According to the WHO, the relation between the incidence of stroke and blood pressure is continuous and steep. [133] All types of stroke (haemorhagic, lacunar and thrombotic gas emboli from gas-producing microbes, oil globules from many depot slow release preparations) are associated with hypertension. The WHO also maintain that plasma cholesterol is not related to the risk of stroke as strongly as hypertension but tobacco smoking, diabetes and obesity are predictors.

In yet another study in the United States, illicit drugs, appetite suppressants, decongestants, and anabolic steroids were found to be likely causes of stroke particularly in young patients through varied mechanisms. [134] For instance, drug - induced vasoconstriction, hypertension or vasculitis probably contribute significantly to occurrence of stroke in most patients, whereas in cocaine abusers, infective endocarditis and most importantly, cerebral aneurysms, vascular malformations and cardiac disorders may contribute significantly[134] Tobacco smoking and heavy chronic alcohol consumption additional independent risk factors for stroke, although moderate drinking appears to protect from stroke in majority of

patients. [134] Finally in this study, it was observed that oral contraceptives increase the risk of thronbotic and haemorhagic stroke in female patient over 35 years of age who also have other risk factors, [134]

Robertson et al (1987), reported that hypertension per se is a major cause of primary intracerebral haemorrhage which accounts for some 20% of strokes. About 80% of this type of bleed occurs in the cerebral hemisphere, 10% in the brainstem and 5% in the cerebellum, and the exact pathology is micro-aneurysm of the intracranial arteries. [135] However the majority of strokes (80%) occur due to cerebral infarction, for which hypertension is an important but less direct predisposing factor. Plaques of atheroma may cause cerebral infarcts, either as a source of emboli or by causing progressive occlusion of cerebral arteries. The infarcts are composed of atheromatous debris and cholesterol crystals or mixtures of fibrin, leucocytes and platelets [136] . There are rare types of cerebral and cerebellar infarcts which occur from sudden blood pressure reduction and consequent cerebral ischaemia at areas of distribution of major cerebral arteries.

Hypertensive Encephalopathy. This describes the convulsions or fits associated with high blood pressure. The patients present with hypertension and coma and with treatment, may make a full and often surprising recovery without evidence of stroke or focal damage. The pathologic changes in this condition may be the lesion of segmental vascular constriction with capillary stasis and oedema as well as a "break through" of cerebral autoregulation, with tissue and vascular damage both related to over perfusion and physical damage to vessel walls, which is maximal in the dilated areas [137] .

Subarachnoid haemorrhage. According to reports it is uncertain how HBP causes subarachnoid haemarrhage. But nevertheless the prognosis is

worse in a hypertensive patient following subarachchnoid rupture of a saccular aneurysm. This situation requires appropriate antihypertensive therapy [138].

Transient ischaemic attacks (TIAs). They are reversible disturbances of cerebral function which last less than 24 hours. They can be due to temporary arterial occlusion by embolism, external compression of an artery (especially at site of ongoing disease), or due to sudden hypotension (e.g cardiac arrythmia). According to reports, 30% of TIAs evolve to a major stroke within 5 years. [138] Also hypertension is a potent factor predisposing to such an adverse sequel. Antitrhombic treatment can reduce TIAs [138].

1.7.2.2 **The Eye**

Examination of the eye using the opthalmoscope has been a traditional way of evaluating the severity and progression of hypertension as well as organ damage in hypertensive patients. But in recent times, simple thickening of retinal arteries is related more closely to age than to blood pressure [139]. In the early stages, the initial arterial consequences of hypertension are seen as irregular thickening and tortuosity of the retinal arteries. Also occasionally retinal circulation, central or sectorial retinal arterial or venous occlusions can accompany high blood pressure and can be readily diagnosed by ophthalonoscope which permits direct inspection of arteries (ophthalmoscopic retinal damage is diagnostic of SBP).[140]

The Keith, Wagener and Barker classification [141] though much criticised has the merit of emphasising the importance of fundoscopy in assessing the progressive arterial diseases of advancing hypertension. The patients are categorised into **group I:** patients with mild hypertension, show minor narrowing or sclerosis of the retinal vessels, **group II:** patients show more severe sclerotic changes, **group III:** patients have retinal haemorrhages,

exudates and oedema, in addition to the arterial irregularities of **group II**, and **in group IV:**, swelling of the optic discs is also evident.

Retinal changes in malignant hyperrtension have been well studied. On flourescein angiography, arteriolar leakage is clearly demonstrable. The onset of the malignant phase can be recognised using the opthalmoscope by the appearance of bilatered retinal exudates which may be circumscribed ("hard') or fluffy ("cotton wool"), haemorrhages and in the later stages, papilloedema and retinal oedema. **Focal micro-infarction**, which occurs in the inner two - thirds of the retina gives rise to the cotton - wool exudates in the nerve fibre layer, and these exudates comprise the swollen bulbous ends of axons (cytoid bodies containing both normal and degenerative organelles; **"Hard" exudates**. These are caused by the accumulation of plasma and lipid in the outer plexiform layer of the retina in the "watershed" zone between the retina and choroidal circulations. In severe cases they form a characteristic "star" around the macula. And Haemorrhages result from pre-capillary ateries and from capillaries tend to be flame-shaped in the nerve fibre layer, and rounded ("blot" haemorrahages) in the outer plexiform layer. **Micro - aneurysms** appear as small evaginations in the capillary wall, and occur when the endothelial cells or pericytes are destroyed by ischaemia Papilloedema is the result of massive interference with axoplasmic flow at the disc. **Elschnigs'** spots are small white areas in the fundus resulting from depigmentation in infracted areas of the pigment epithelium.

1.7.2.3 **The Kidney**

The Kidney is an important target of hypertension - induced organ damage. Severe and malignant (accelerated) hypertension often leads to renal insufficiency, as a consequence of fibrinoid necrosis of small arteris, within

a few years. But in less severe forms of hypertension, renal damage caused by ateriosclerosis is mild and develops slowly [142]. Renal damage due to hypertension is commonly preceded by proteinuria, (greater than 300mg per day). **Micro - albuminuria** describes abnormally high urinary albumin excretion (30 - 300mg/day) in the absence of clinical protenuria. Also protesinuria has been found to be an independent risk factor for mortality due to several causes as well as cardiovascular disease [143].

Guyton et al (1983) observed that salt and water retention tended to occur except the kidney is perfused at higher arterial pressure. [144] This explains why some workers link arterial and arteriolar wall hypertrophy to "renal barostat" in hypertension. This concept is regarded to be relevant in the pathogenesis of the raised blood pressure. And according to Robertson et all, arterial and arteriolar narrowing in the kidney due to hypertension has been invoked as the cause of the upward re-setting of the levels of systemic arterial pressure which can induce niatriueresis ("Pressure natriuresis").

During the malignant phase of hypertension renal lesions which occur are serious, with extensive and progressive fibrinoid necrosis of afferent glomerular arteriles glomerular infarction and resultant renal impairment, in a majority of patients. Thus if malignant hypertension is left untreated, the patient eventually succumbs to renal failure (with urinary incontinence, renal lesion such as proteinuria, haematuria and granular casts), if a catastrophic cerebral lesion or cardiac failure do not occur to terminate its course abruptly. However, if hypertension is not at the malignant phase, the clinical effects on the kidney are not prominent. But the decline in renal function with age is faster in the presence of a raised arternal pressure and atheroma of the renal artery is the commonest cause of renal artry stenosis. [145]

1.7.2.4 The Heart

Left ventricular hypertrophy is an early and consistent feature of hypertension. This is associated with enlargement of cardiac myocytes as well as an increase in their numbers. **Consentric hypertrophy** is increase in wall thickness without corresponding enlargement

of the ventricular cavity. **Eccentric-hypertrophy** is the enlargement of the ventricular cavity without increase in the ratio of wall thickness to chamber size despite an increase in left ventricular mass.

Several workers have speculated that although left ventricular hypertrophy is initially adaptive and thus beneficial, later, left ventricular relaxation lusitropy and filling are impaired and ventricular compliance is induced due to increased collogen deposition[145] This causes increase in end diastolic pressure. It also causes reduction in the number of andrenoceptors with resultant dependence on the Frank - Starling mechanism to maintain cardiac function (less dependence on neurohomonal mechanism). This is the reason why hypertension progresses to cardiac failure, and sub endocardial ischaemia is frequent because coronary filling during diastole is impaired in left ventricular hypertrophy.

Carotid arteries. There is well known increase in the prevalence of atherosclerotic complications in hypertensive patients due to an increased incidence of atherosclerotic lesions in the carotid arteries. And severe carotid stenosis frequently causes stroke. Just as ulceration of the plaques can form emboli which provoke ischaemic strokes or TIAs. The carotid arteries, presence of plaques and their nature, rate of growth and extent of stenosis can be evaluated using echography and Doppler ultrasound instead of the older invasive angiographic techniques [146]. According to Robertson et al [147] cardiac impairment in hypertension may be partially due to hypertrophy of the surrounding of coronary arterioles or of coronary arteriolar fibrinoid necrosis in malignant hypertension. Other workers propose multifocal ventricular myocardial necrosis caused by high circulating concentrations of angiotensin II or catecholamines [148]. There is little evidence of left ventricular hypertrophy in patients with mild HBP and their pressure elevation is supported by increase in myocardial contractility rather than by ventricular hypertrophy. It has been found that concentric hypertrophy characterises established hypertension without cardiac impairment. While eccentric hypertrophy is associated with incomplete systolic emptying [148] Through echocardiography, workers have reinforced the electrocardiograph findings that left ventricular hypertrophy is associated with increased morbidity and mortality, mostly due to cardiac abnormalities especially LVH And ventricular ectopic rythms were more prevalent in the presence of hypertensive left ventricular hypertrophy, LVH.

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Coronary reserve. Evidence is increasing that coronary flow reserve, (maximum capacity to increase coronary blood flow), is often reduced by about 30 - 40% in hypertensive patients, even when there is no stenotic lesion of the epicardial coronary arteries. Furthermore, cardiac biopsy has suggested that structural alterations and not purely functional changes of small (resistance) coronary arteries may be largely responsible for this limitation of coronary reserve [149].

Myocardial infarction. It is known that episodes of myocardial infarction and sudden cardiac death are increased in hypertension. And presently, it is know that much of the increased incidence is due to atherosclerotic lesions of large coronary arteries, LVH, myocardial fibrosis or disease of small coronary arteries [150]

Congestive Heart Failure. Epidemiological studies on heart failure show that congestive heart failure, CHF, has become an increasing and frequent reason for hospital admission during the past 2 decades [151], and this represents a major health problem. Data from the Framingham heart study indicate that the incidence of CHF increases with age and **is higher in men than in women** [151] Hypertension and coronary heart disease are the two most common conditions that predate the onset of CHF. Diabetes mellitus and LVH are also associated with an increased risk of heart failure. This study found that in the decade of 1980, the annual age-adjusted incidence of CHF among people 45 years and above was 7.2 cases in 1000 (male) and 4.7 in 1000 (female). Also, the mortality with CHF was high, with median survival time of 1.7 years in men and 3.2 years in women, and a 5 - years survival rate of 25% in men and 38% in women. According to the WHO report, untreated hypertension may lead to congestive heart failure, and before the institution of effective hypertensive therapy, CHF was one of the commonest complications of hypertension. Progressive enlargement of the left ventricle, coupled with coronary artery disease act in concert to complicate the hypertensive disorder and make the overall management difficult. Meta analysis of controlled clinical trials which include those on HBP in the elderly, indicate that antihypertensives can reduce the incidence of CHF by about 50% [152]. Other risk factors for development of CHF are recognised such as race, (Black hypertensive patients reported

to be especially prone to CHF reasons for this not sufficiently understood), and a form of dilated cardiomyopathy with biventricular failure described in Africa hypertensives. Occasionally, left ventricular failure has been observed in hypertensive with small hearts and severe diastolic dysfunction. These factors can be corrected [153].

Heart Failure. Hypertension is known to produce both subtle and pervasive effects such as those on left ventricular morphology and function. And the increased workload imposed directly by raised arterial pressure, decline in ventricular adrenoceptors; diminished coronary reserve and possible myocardial necrotic lesions; all of these promote development of cardiac failure. From the Franmingham Heart study, age - adjusted prevalence of overt heart failure was 24 in 1000 (men) and 25 in 1000 (women). And despite improved treatment for ischaemic heart disease and hypertension, the age adjusted incidence of heart failure has only declined by 11% per calendar decade in men and by 17% per Calendar year in women, during a 40-year period of observation. [153]

Coronary artery atheromatous disease

Workers have suggested that coronary artery atheroma is one of the most frequent pathologic feature of raised arterial pressure, [154] being common in mild hypertension. In mild hypertension, coronary artery disease is more common than stroke and cardiac failures, suggesting a strong correlation between HBP and atheromatous coronary artery disease (CAD).

1.7.2.5 **Other Diseases**

Diabetes mellitus. It is associated with vascular lesions and its co-existence with hypertension increases the risk of vascular disease. Viberty (1990) [155], a Professor of Diabetic medicine in London, observed that diabetes produces a perturbation of the external milieu by increasing a number of growth factors resulting in an enhanced cell growth or proliferation in response to mitogens. This is associated with an overactivity of the sodium - hydrogen antiporter, which is related to the hypertrophic and hyperplastic changes that take place in the smooth muscle cells and in other cell types. He has also stated that these changes are associated with insulin resistance, which may be a consequence of increased

growth. Also he found that an increase in sodium - hydrogen antipathy produces retention and increased intracellular sodium and calcium concentration, leading to increased vascular tone. The hypertrophic, hyperplastic changes, lead to organomegaly, left ventricular hypertrophy, kidneys and mesangial expansion, and vascular hypertrophy. Increased vascular tone and hypertrophy contribute to hypertension. He also suggested that lipi disturbances as a consequence of hyperinsulinaemia, combine with vascular hypertrophy to produce some the lesions of atherosclerosis. He concluded that hypertension, atherosclerosis, and glomerular sclerosis explain why insulin dependent diabetes with the susceptibility factor, develop renal failure and excess cardiovascular disease [156].

Insulin resistance. According to Defronzo a Professor of Medicine and Chief, Diabetes Division in Texas, University, United States, insulin resistance is an integral part of the ageing process. With age, body tissues become less responsive to insulin and all metabolic problems such as obesity, diabetes and HBP become more prominent. He also suggested that the insulin resistance syndrome is partly responsible for the development of atherosclerotic cardiovascular disease, dyslipidaemia, increase in rely low-density lipoprotein (VLDL) and LDL cholesterol and decrease in HDL cholesterol. And a likelihood that the compensatory hyperinsulinaemia that occurs in response to the insulin resistance plays a major role in the development of these abnormal cardiovascular risk factors (syndrome of insulin resistance: obesity, diabetes, hypertension, hyperinsulinaemia, hyperlipidamia and ASCVD: atheroschlerotic cardiovascular disease).

Insulin Sensitivity. The insulin clamp technique was developed as the gold standard for measuring insulin action in humans: Normal insulin sensitivity is based on a pressure of glucose utilisation mg per kg of body weight per minute in a healthy control population. An individual that metabolises **more** glucose than the controls, then that person is insulin - sensitive. But if an individual metabolises **less** glucose than the controls he is insulin-resistant as is the case with **Non-insulin dependent diabetes**, **NIDDM** or **Type II diabetes**. De-Fronzo further suggests that, in contrast to what is in most texts, that type II diabetics are not hypoinsulinaemic, but are in fact, significantly hyperinsulinaemic for most part of their

lives. They are however diabetic because they do not secrete sufficient insulin to overcome the insulin resistance thereby maintaining normal glucose tolerance. Furthermore, they secrete more insulin than normal subject in the population. In NIDDM, genes for insulin resistance are inherited. The beta cells of the pancreas recognise the resistance of insulin receptors to insullin, and responds by over-secreting insulin. The resultants state of hyperinsulinaemia, leads to development of hypertension, dyslipidaemia as well as the development of athrosclerosis, independent of blood pressure and lipids ------ the insulin resistant syndrome (Fig. 1.2).

Figure 1.2

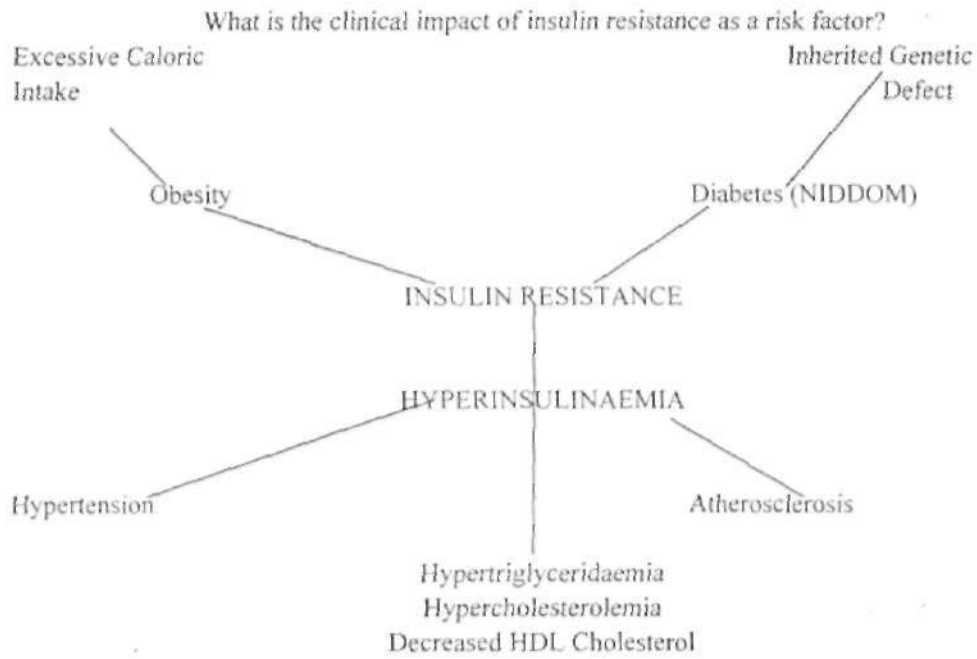


Figure 1.2: The Suggested relationship of insulin resistance with common metabolic disorder.

Epidemiologic studies suggest a strong association between hyperinsulinaemia and hypertension. Where higher insulin concentrations, in all subjects receiving an oral glucose tolerance test, (OGTT), were associated with elevated blood pressure, (both SBP and DBP), as well as higher triglycorides and lower HDL cholesterol. Based on the studies, other workers including Ferrannini et al [157], suggested that hypertension is related to an insulin - resistant state. Because when they compared a group of essential hypertensive individuals with euglycaemic insulin clamps and compared them to a group of normal - weight normotensive controls, they found insulin resistance in the essential hypertensive individuals (pretabolised about 40% less glucose than appropriate

controls). They however concede that not all people with essential hypertension had insulin resistance, and that some people in the normal population were as insulin - resistant as the hypertensives, and the diabetics. In a subsequent study involving 143 lean hypertensives, Pollare et al [158] confirmed the finding of Ferrannini et al and concluded that approximately 60% of essential hypertensive individuals are also insulin-resistant. These studies reveal that the extent of insulin resistance was inversely associated with the plasma insulin concentration, and hyperinsulinaemia was associated with a higher blood pressure. In addition, after studying the molecular mechanisms involved in insulin resistance, the major reason for the insulin resistance was a defect in glycogen formation not in the glucose oxidative pathway. Also people with essential hypertension have the minor beta cell responds to the defect in glucose metabolism by over-secretion of insulin, the compensatory high circulating levels of insulin act as the **sodium proton pump** to enhance sodium flux into the cell and hydrogen ion out. An increase in intracellular sodium now sensitizes the vascular smooth musculature to pressor effects of catecholamines, resulting in the development of hypertension. Insulin also stimulates the **calcium ATPase pump** to increase intracellular calcium, which also causes vasoconstriction resulting in hypertension. The scenario thus being: the game for insulin resistance prompts beta cell over-secretion of insulin which in turn affects the sodium proton pumps as well as the calcium ATPase pump. The increase in intracellular sodium and calcium cause, vascular smooth muscles hyperactivity leading to hypertension. Activation of the sodium proton pump also causes the intracellular pH to rise, and being a growth factor for cell hypertrophy, is responsible for the characteristic lesions in hypertension. Insulin itself is a growth factor and like growth homone stimulate a host of other growth factors especially IGF.1 (immunoglobulin F-1). IGF-1 also causes cellular hypertrophy. The narrowing of the vessel lumen by cellular hypertrophy (and atheroma) impedes blood flow, and increases vascular resistance, thus resulting in elevation of blood pressure. There is only one known genetic defect, which is over-expression of the sodium proton pump, in essential hypertension and it occurs in about **image** of what is seen in type II diabetes **and** obesity. Thus suggesting that the same underlying metabolic

defect is responsible for those three insulin - resistant states. According to Landsberge and associates [159], HBP may result from metabolic disturbance characterised by insulin resistance. They confirmed earlier findings that insulin can cause an increase in the blood pressure by **Stimulating the sympathetic nervous system.** In their case they found that with increasing levels of insulinaemia, there was a progressive increase in the circulating norepinephrine, which was associated with increase in both blood pressure and pulse. This is because the sympathetic nervous system directly innervates the vascular smooth musculeture, with direct vasoconstrictor effects, resulting in an increase in blood pressure. Also the sympathetic innervation of the kidney leads to sodium retention, an increase in total body sodium, content and an increase in blood pressure. These studies document that insulin, by activating the sympathetic nervous system, can cause an increase in blood pressure. Also insulin can cause an increase in blood pressure by altering cellular sodium pumps, which reside in the vascular smooth muscles (the sodium proton pump). This sodium proton pump is present in all cell membranes and is a stimulator of this pump. Half of the people with this defect, (which can take any of several forms), could be hyperinsulinaema with normally functioning sodium proton pump, or a normal insulin level with over expression of sodium proton exchanger. or both the insulin resistance gene and over expression of the sodium proton pump hence pertinently predisposed to developing hypertension. All these conditions lead to an increase in intracellular sodium, vascular hyperactivity and hypertension. Lastly, hyperinsulinaemia can cause the lipid abnormalities which are associated with atherosclerosis. WHO studies have established the common co-existence of hypertension and NIDDM, [160]. and patients with both these conditions are especially vulnerable to cardiovascular and renal complications; therefore, the control of hypertension and dyslipidaemia - and the cessation of smoking, are considered to be very important aspect in the management of hypertension.

1.8 PRESENTING COMPLAINTS

The WHO list symptoms of organ damage as those affecting the **Brain and Eyes** such as headache, vertigo, impaired vision, transient ischeamic attacks, impaired vision, transient. Those that affect the heart, include palpitation, chest pain, shortness of breath, swollen ankles. While symptoms of kidney damage include thirst, polyuria, nocturia, haemoturia of **peripheral arteries,** there are symptoms as cold extremities, intermittent claudiation. These symptoms can be obtained by carefully taking patient history, such that important information about concomitant risk factors, symptoms of organ damage and hints secondary hypertension can be obtained [161].

1.9 DRUG HISTORY AND HYPERTENSION

Antihypertensive therapy is directed to the prevention or correction of disorders such as malignant hypertension, hypertensive encephalopathy, cardiac failure, stroke, coronary heart disease and progressive impairment of renal function [162]. The effectiveness of treatment has been evaluated with progressive reformation in the introduction of drugs capable of lowering arterial blood pressure in the 1950s. From which time almost all the progress in this respect has been derived from pharmacotherapy. But there has been steady and increasing interest in non-pharmacological means of blood pressure reduction. The goal of treatment as suggested by the WHO should be the maximum tolerated reduction in blood pressure [162] This is because it has been shown from epidemiological studies that, within the normal range of both SBP and DBP, the lower the blood pressure, the lower the risks of both stroke and coronary events. Preuss et all [164], has shown that hypertension which is more prevalent with aging, is a major risk factor for other cardiovascular disorders, accordingly therefore, it is important to decrease blood pressure and maintain it within an acceptable range to reduce morbidity and mortality. When non-pharmacological therapy fails, drug therapy should be additionally instituted. The effective drugs they suggest, are those which lower blood pressure have few adverse side effects and may have additional benefits on co-existing maladies. An interesting study [165] which involved use of the assessment of the quality of life to evaluate medical treatment in an effort to conserve resources and limit

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costs was conducted in 1973. It was called the Gotenberg Quality of life assessment. It was based on responses, from men born in 1913 (50 years old at the time of the initial survey 1963), and re-evaluated 10 years later. The WHO definition of health or well-being was the source of the 15 factors which were used for the assessment. A questionnaire of 30 symptoms relating to the most common elements of physical, mental and social well-being were administered. The assessment was validated by termination of the variation in the physical, mental and social components of well-being based on age. And when this was applied to subjects with cardiovascular disease, significantly lower quantity of life scores especially regarding general well -being, fitness and energy of subjects with hypertension and congestive heart failure when compared to subjects without these diseases. But when the assessment was evaluated as a risk factor for cardiovascular disease and mortality, the results of univariate analysis shared that health, fitness and appetite were significantly correlated with total mortality, while multivariate analysis indicated that only health was a significant factor.

Many studies on the value of treating hypertension have been conducted in the elderly, such as the results of three major international trials against hypertension in the elderly published in 1991 and 1992. These were the Systolic Hypertension in the Elderly Program (SHEP) from the United States, the Swedish Trial in Old Patients with hypertension (STOP-hypertension) from Sweden and the Medical Research Council (MRC) trial. Patients with both systolic and diastolic hypertension were recruited. In all three trials, diuretics and/or beta-blocks (frequently used in combination) formed the basis of active treatment. And the patients were randomly allocated either to active treatment or to a placebo. The therapeutic results showed that for all three trials showed clear benefits from actively lowering elevated arterial pressure in patients aged 60 years or more. In particular, fatal and non-fatal strokes were significantly reduced. In the SHEP trial , fatal and non-fatal myocardial infarction and coronary disease were also reduce and in the Stop trial total mortality was markedly reduced [166]. There is a general agreement as, provided by the WHO/ISH (world Health Organisation/International Society of Hypertension), guidelines; that five classes of drug are most suitable for the first-line treatment of patients, with hypertension [167 a,b] . These include diuretics, beta -blockers, ACE inhibitors, calcium antagonists and alpha -blockers. But other classes of drugs may be used in certain situations. For instance, Italian researchers recently found that consuming vitamin C may also help by easing, vessel constriction in high blood pressure patients. so they suggested a diet with more fruits, more

vitamin C and possibly vitamin C supplements [168]. Also hypertension optional treatment (HOT) study, suggests the use of low dose aspirin (75mg once daily) in hypertensive patients whose blood pressure has been rigorously controlled, who are at high risk of coronary heart disease (CHD), and not at risk of bleeding from the gastrointestinal tract or from other sites [169]. But there is a recent addition to the WHO/ISH list of first-line antihypertensives which brings the total to six main drugs classes. It is the classes of Angiotension II antagonists. The WHO recommends that all these classes of drugs are suitable for the initiation and maintenance therapy for lowering blood pressure. But the choice of drugs, they allow can be influenced by cost and many other factors (such as compelling indications, possible indication, compelling contraindications and possible contraindications) for special groups of patients. For instance, in some parts of the world reserpine and methyldopa are also frequently used [170]. In addition, there is more evidence of beneficial effects on morbidity and mortality from randomised controlled trials with older antihypertensives such as diuretics and beta-blockers, but evidence of benefit with newer drugs such as ACE - inhibits and calcium antagonists is beginning to accumulate.

1.9.1 Diuretics

These have been widely used as first-line antihypertensive drugs. They have been shown to prevent cardiovascular morbidity and mortality especially fatal and non-fatal stroke [171]. But large doses may produce unwanted metabolic effects (potassium depletion, reduces glucose tolerance, ventricular atopic beats and impotence) [172]. But these can be reduced by keeping the dose as low as possible. Low dose diuretics remain effective not only lowering blood pressure but also reducing cardiovascular morbidity and mortality as shown in recent trials in the elderly [173]. Another advantage of diuretics is that they are inexpensive and enhance the effectiveness of other types of antihypertensive drugs. The antihypertensive effects of orally effective diuretics has been demonstrated in all the commonly used thiazides and related drugs as well as for the more powerful loop diuretics (frusemide, ethacrynic acid and xipamide), and the potassium -sparing agents (amiloride, spironolecture, canrenoce and triamterene). Generally, the longer acting thiazide (bendrofluazide or hydrochlorothizide) do not have an abrupt and potent diuretic effect and this makes them the most appropriate

on the treatment of essential hypertension. Except in cases of renal, cardiac impairment or resistant hypertension which require a loop diuretic [174].

1.9.2 **Sympatholytics**

These include those altering central sympathetic activity, andrenergic neurone blockers, andrenergic receptor blockers (Beta receptor blockers and Alpha receptor blockers), ganglion blockers and monoamine - oxidase inhibitors.(MAO-I)

Adrenergic Neurone - Blocking Drugs. This class of drugs succeeded the earliest effective antihypertensives (autonomic ganglion blockers). They include bretyliom, quanethiadime, bethamidine and debrisoquine. These are highly concentrated in andrenogic nervous, blocking neutotransmitter release. Thus they combined the disadvantages of unopposed parasympathetic discharge with sympathetic blockade. Thus their administration was characterised by postural hypertension. But they have now passed out of clinical use [175].

Autonomic Ganglion - Blocking agents. Their development was the logical step from the surgical therapy such as bilateral dorso-lumbar sympathectomy. And their introduction represented one of the major therapeutic advances of this century [176]. But the sympathetic blockade meant that ganglion blockers, to be effective, had a marked postural hypertensive effect; their parasympathetic blocking actions induced constipation, dryness of the mouth and occasional paralytic Ilheus. They have since passed out of clinical use. These are examplified by Trimetaphan and Pentolinium.

Centrally Acting Drugs. This class consists of three major drugs, methyldopa, clomidine and reserpine **Methyldopa**, has been valuable in the treatment of HBP. Though obsolete in other parts of the world still remains widely used, in some parts of the world. It is thought to lower blood pressure by inhibiting the enzyme - dopa - decarboxylase, thereby limiting the synthesis of catecholomines. Also noradreline in sympathetic nerve terminals is replaced by alpha-methyl-noradreline, a much weaker agonist than noradreline itself ("false transmitter" concept). Also, its metabolite alpha methyl noradreline, has central nervous system effects especially alpha - 2 adrenergic agonism, depressing sympathetic nerve discharge. All those mechanisms contribute to the reduction of blood pressure by methyldopa. Methyldopa produces mild but distinct additional fall in pressure in standing with modest slowing of

heart rate side - effects include drowsiness, dryness of the mouth nasal stuffiness, postural hypotension, rashes and diarrhea. It has been useful in pregnancy hypertension, and in the elderly [177]. But it does not produce rebound hypertension when discontinued.

Clonidine. It appears to act through centrally mediated selective alpha - 2 adrenoceptor i.e agonist effect leading to inhibition of sympathetic neurotransmitter discharge. It lowers arterial pressure with a distinct reduction of heart rate but with less postural hypotension. It side effects include dryness of the mouth somnolence and constupation. If suddenly stopped, there follows excessive sympathetic discharge for 1 - 2 days, with excess of circulating catecholamines tachycardia, rebound hypertension and headache. This attack can be treated promptly by re-starting chliodine or by administration of alpha-receptor blockers alone or by administration of both alpha - and beta - adrenergic receptor blockers. Recently, clonidine has been given transdermally rather than orally (adhessive polymer designed to release clonidine over 1 week over the chest or upper arm). But skin reactions were reported in upto 25% of the patients given clonidine by patch application, also rebound hypertension was noticed after removal of the clonidine patch [178].

Reserpine. This is a rauwolfia alkaloid which depletes noraderenaline stores in sympathetic nerve terminals both within the central and peripheral nervous systems. It produces cummulative effect which may persist for several weeks after therapy is discontinued. It produces minimal postural hypotension even though there is bradycardia along with lowering of blood pressure. Side effects include nasal stuffiness, diarrhea, drowsiness, lethargy and occasional frank depression with suicidal tendencies. It is widely prescribed in the USA, Germany and Switzerland but because of the depression was not widely used in Britain [179], though depression is uncommon with the low doses prescribed.

The use of reserpine, ganglion blockers and other older drugs is now limited to certain special cases (such as control of hypertension in surgery) And therapy should be individualized preferably with ration combination.

Alpha - adrenoceptor blockers. - this class include drugs such as phenoxybenzamine, phentolamine, prazosin etc. These are safe and effective in lowering blood pressure. The main side effects is postural hypertension after the first dose which is especially problematic in the elderly or patients with autonomic neuropathy [180]. There is some evidence that alpha

adrenoceptor blockers may be of advantage in patient with hyperlipidaemic or glucose - intolerance [180 a,b],. but there are no long - term clinical trials demonstrating reduction in morbidity or mortality in hypertensive patients treated with this class of drugs. It is usually necessary to assess patient blood pressure in the standing position for those receiving alpha blockers such as phentolamine (non – selective) which produces marked postural hypertension, tachycardia and diarrhoea. Barazosin however has selective post - synaptic alpha - 1 blocking effect. Longer - acting related drugs such as tetrazosin and doxazosin have been develped. These agents produce first - dose, postural hypertension which is frequent, unpredictable and severe, except if very small doses are used. With further treatment mild postural hyportension which is associated with tachycardia may be produced. These effects have limited their use especially in the elderly. However, the lack of disturbance of serom-lipids and other less serious side - effects are seen as an advantage. Indoramine is another effective alpha - 1 receptor blocker but has unwanted action such as drowsiness, nasal stuffiness and dryness of the mouth reported as side effects. Alpha blockers are generally used as supportive therapy rather than monotherapy in essential hypertension and also used in phaechromocytone.

Beta - adrenoceptor blockers. Beta - receptor blockers were discovered by an astute clinical observation [185a,b]. These are safe, cheap and effective. They are widely used in patients of all ages with different degrees of severity. They have formed the treatment regiment in many of the major studies which have demonstrated reduction in morbidity and morality attributed to reduction of blood pressure [182]. A large variety of beta - blockers are available - some are cardio - selective while others have intrinsic sympathomimetic activity or alpha - blocking or vasodialatory action [183]. Beta-blockers have also been shown to be useful in preventing myocardial infarction [184], second - line drug of choice as they have not been shown to have any advantage over diuretics in the primary prevention of myocardial infarction in hypertensive patients. They are first - line drugs of choice with thiazide diuretics for many doctors. Another standard combination is the triple combination of diuretic, vasodilator (e.g hydralazine) with a beta - receptor blocking drug. Their mode

of action include lowering blood pressure through a central nervous effect of diminishing sympathetic outflow; reduction of cardiac output; diminution of renin secretion and pre-synaptic action of inhibiting release of neurotransmitter. Not one of these explanations acts alone but a combination of all, these may serve to explain the action of beta - blockers. The **cardioselective beta - receptor blockers** include atenolol, practolol, metoprolol, tolamolol. Those with **Intrinsic - Smpathomimetic Activity** (ISA) include propranolol, oxprenolol, pindolol, nadolol [186]. A study to evaluate the effect of current treatment with non - selective or cardioselective beta - blockers on the outcome of a first acute myocardial infarction in hypertensive patients. Using retrospective analysis of the data collected from a continuously operating register of all hospitalised acute myocardial infarction patients in Sweden; 323 patients were treated with a non - selective beta - receptor blockers and 338 with a cardioselective beta - receptor blocker[183] In patients receiving non-selective beta - blockers the mean peak aspartate aminotransferase was long than the peak recorded in patients who received cardioselective beta - blocker. The study after correction for several clinical characteristics, concluded that current treatment with non - selective beta blockers may have reduced the enzymatically estimated infarct size and the occurrence of circulatory arrest due to ventricular tachyarrythmias. Both non - selective and cardioselective beta - blockers may also have reduced the hospital in-patients mortality.[187] In a related clinical study using adrenaline infusions in healthy volunteers, they found that beta - 2 adrenoceptor blocker improved potentially arrythomogenic variables, such as hypokalaemia and hypomagnesaemia. But the adrenaline - induced reduction in diostollic blood pressure was reversed. But pre - treatment with the new beta - blocker called carvedilol was found to preserve the beneficial electrolyte effects without increasing blood pressure during the adrenaline infusion.

Monoamine - oxidase inhibitors. (MAO – I) This group includes non - hydrazine derivatives such as pargyline used in certain forms of hypertension. They act on adrenergic neurones and cause production of "false transmitter". They cause serious drug interactions with both drugs and foods which contain indirectly acting sympathomimetic amines, (tyramine in cheese wines and other food). In the presence of MAO - I, these amines cause

massive release of noradrenaline and other amines, this could result in hypertensive crisis. .There seem to be two forms of MAO - I with difference substrates and different sensitivity to selective inhibitors. Clergyline though structurally related to pargyline has been introduced to treat hypertension. MAO - A deaminates physiological substrates such as 5 - Hydroxytryptamine, (5 - HT), noradrenaline, adrenaline, metaniphrine and normetanephrine. MAO - A occurs in high concentration in the gastrointestinal tract and liver while MAO - B is abundant in platelets. Clorygyline is still under investigation and there are claims that it produces less side effects. The use of MAO - I is still controversial [188]

1.9.3 **Angiotensin Converting Enzyme Inhibitors (ACE - I).**

This class of anti-hypertensive drugs acts on the renin angiotensin system. Only the orally effective members have become established in treating hypertension. **Angiotensin – I antagonist** LOSARTAN antagonis effect of angiotensin - I on angiotensin I receptor competetively. **Angiotensin II analogue antagonist** such as saralasin must be given intravenously, so they have little therapeutic value. **Renin inhibitors** are expected to lower blood pressure by decreasing level of angiotensin II. It has been administered parenterally in clinical trials in man, but oral forms are yet to be developed [189]. The third class is called the **Angiotensin converting enzyme inhibitors**. There is a range of orally active forms of this class [190]. Some such as captopril and lisinopril are taken in their active form. others such as enalapril and ramipril are administered as pro-drugs (de-esterified in the liver to the active forms analaprilate and remiprilate, respectively). These forms are eliminated by the kidney and hence the doses need to be reduced in impaired renal function. They all produce dose-dependent fall in circulatory plasma angotensin II, and also in tissue especially arterial smooth muscle. They are also called **peptidyl dipeptide inhibitors.** ACE - Inhibitors have been found to be safe and effective in reducing blood pressure. They are well tolerated by most patients and have no metabolic side effect, the most common one being a dry persistent cough; a rare but serious side effect called angiooedema. ACE - Inhibitors are to be avoided in pregnancy especially in the second half of it because they may cause fetal and neonatal death [191]. ACE - inhibitors have been shown to decrease morbidity and mortality, (coronary

events), in patients with congestive hearth failure and after myocardial infarction with reduced ejection fraction [192]. They prevent left ventricular dilation and reduce development of left ventricular hypertrophy in hypertensives. And also delays progress of renal disease in patients with insulin - dependent diabetes mellitus and moderate renal impairment [192]

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1.9.4 **Calcium Channel Blockers**.

Also called calcium antagonists. These consist of several groups, class I: **phenylalkylamines** such as verapamil. They are capable of lowering blood pressure without postural hypertension. It reduces atrio-ventricular conduction thus reducing heart rate. The drug is used with caution in older patients who are also taking beta - blockers as profound bradycardia or cardiac arrest may result [194] . Class II members such as dihydropryridines (nifedipine, isradipine, nicardipine). They have been extensively used to treat hypertension. They produce different extents of arterial dilation in various organs. They are rapidly absorbed and have a short duration. So if sufficient dose to give prolonged effect is given to a patient excessively, high blood levels can result producing marked side effects. The effects of nifedipine is enhanced by concurrent administration of cimetidine with adverse effects such as headache, nausea and tachycardia early in therapy even though they subside later. However, facial flushing may persist and ankle oedema may occur without appreciable weight gain. Calcium antagonist produce modest duresis and natriuresis but without significant decrease in body weight or of total body sodium by the third month on a study with nicardipine [195] . Class III drugs include Diltiazem with less side effects except troublesome rashes. Class I - III lower peripheral vascular resistance by blocking calcium ion transfer into the cells of vascular smooth muscle and the myocardium. Though calcium antagonists do not appear to have adverse metabolic effects their safety profile has not yet been established in early pregnancy [196] . And according to the WHO there is no evidence from long - term trials that they can lower morbidity or mortality in HBP.

1.9.5 Vasodilators

Many antihypertensives dilate resistance vessels (arterioles) but vasodilators are those which produce a direct effect on vascular smooth muscle. They include hydralazine, minoxidil, diazoxide and nirtoprusside.

Hydralazine has been used for many years in the "standard" triple therapy involving a diuretic and beta receptor blocker- Beta blockers were used for their action on strong heart rate which was useful in reflex tachycardia caused by vasodilation with hydralazine. It does not cause postural hypertension, but can cause fluid retention and in very high doses (over 200mg) a syndrome of fever, weight loss, joint pain, arthritis and rashes (like lupus erethematosus) but rarely, it can cause pleurisy, pericarditis and splenomgaly. Haemoglobin levels may fall, lupus cells appear in the blood and erythrocyte sedimentation rate is increased. Slow acetylators of hydralazine are prone (12% women and 3% of men during long - term treatment) sometimes hydralazine can cause hersutism. But it remains a valuable drug any and in one comparative trial of range of adjuncts to beta - blockers plus thiazede treatment, was found to be best in terms of efficacy and side - effects [197].

Minoxidil. Is more powerful than hydralozine and reserved for resistant hypertension where it is very effective. It causes marked fluid retention and tachycardia compared to hydralazine and so it is usually given with a beta - blockers and a loop diuretic but if patients can not tolerate beta-blockers, (brocho spasm, or peripheral vascular disease), methyldopa or an ACE - inhibitor or oerapanil can sometimes control the tachycardia. Its major disadvantage is hirsutism which can hurt its use in female patients.

Diazoxide. It is a powerful vasodilator which even though very effective is not much in use because it causes hyperglycaemia as well as tachycardia and hirsuitism.

Nitroprusside. Is the most potent, predictable parenteral antihypertensive. Its nitroso group dilates arterioles and veins. Unlike hydralazine, minoxidil and diazoxie) it increases venous capacitance and so reduces preload as well as afterload, but does not block autonomic transmission [198]. In heart failure it improves left ventricular function by reducing diastolic and left ventricular pressures. It is used in hypertensive emergencies to produce minute by minute control of blood pressure. It also improves angina and maintains renal blood flow

anglomenular filtration rate. During prolonged therapy its metabolite thiocyanate can accumulate and if it exceeds 10mg/dl toxemia may occur and therapy must be discontinued. But blood pressure returns to pretreatment levels within 10 minutes of stopping nitroprusside infusion other arteriolar/venous vasodilators are pinacidil, cromakalin. These are also potasium channel openers being tried for treatment of hypertension.

1.9.6 **Drug Combinations**.

If a drug from any of the six drug classes is ineffective in lowering blood pressure for a given patient, the WHO recommends substitution of a drug from a different class. And if therapy with a single drug (monotherapy) is only partially effective, it may be preferable to add a small dose of a second drug from another class rather than increase the dose [199] . This permits addition of different primary actions while minimising the homeostatic compensations that limit the fall in pressure. Combination therapy also reduces side effects by encouraging the use of drug on low doses. For instance centrally acting drugs have worse side effects than other classes, though they are relatively cheap. So if they are used in low income populations because if their cost effectiveness (reserpine, methyldopa) it is recommended to use than in combination with diuretics and to prescribe centrally acting antihyhypertensives in much lower doses than in earlier years. Also, direct vasodilators *(hydralazine, minoxidil) though effective for reducing blood pressure, are not commonly* used because of their side effects. **Additive** effect have been shown with such combination as a diuretic with a beta - blocker, ACF - Inhibitor or alpha - blocker; a beta - blocker with an alpha - blocker or a dihydropyridine calcium antagonist; an ACE - inhibitor with a calcium antagonist. So, in order to maximise the benefits of treatment in all hypertensives *combinations of two or up to three drugs may be required.* Also, *for reasons of convenience,* cost and increased patient compliance, some preparations are manufactured to contain two drugs in a single tablets or capsule. Such preparation may be appropriate for many patients once the need and dose for constituents drugs have been established.

1.9.7 **Choice of Drug for Hypertensive Patients**.

The choice of antihypertensives will depend on amongst other things socio-economic factors which determine availability in different countries or regions and the characteristics of the individual patient (especially risk factors, target organ damage, co-existing illness and possible side - effects). According to the WHO [200] guidelines, for selecting drug treatment of hypertension; all the six drug classes can be used to initiate and maintain blood pressure reduction depending on other factors as well as cost. For diuretics, compelling indications are heart failure elderly patients, systolic hypertension; the possible indication is diabetes mellitus, to compelling contra - indications is gout and possible contra indication is dyshpidaemia and of well as sexually active males. For Beta blockers, compelling indications include angina, after myocardial infarct, tachyarrhythmias; possible indications include heart failure, pregnancy and diabetes; compelling contraindications are Asthma and chronic obstructive pulmonary disease and grade 2 or 3 atrio-ventricular heart block; with possible contra - indication being dyslipidaema, Athletes and physically active patients, peripheral vascular disease. For ACE - inhibitors, compelling indications are heart failure, left ventricular dysfunction, after myocardial infarct and diabetic nephrophathy; the compelling contra indications are pregnancy, bilateral renal artery stenosis, hyperkalemia. Calcium antagonist, compelling indications are peripheral vascular disease; compelling centraindicators are Grade 2 or 3 atrioventricular block with verapamil or diltiazerm; possible contraindication is congestive heart failure Alpha - blockers; compelling indication is protatic hypertrophy; possible indication are glucose intolerance dyslipideamia and possible contra- indiaction is orthostatic hypotension.

Angiotension II antagonist has compelling indications such as side effects with other drug classes, for example ACE inhibitor cough; possible indication is Heart failure and compelling contraindications are pregnancy bilateral renal artery stenosis, hyperkalimia.

1.9.8 **Stepped - Care and the Concept of Drug Combinations**.

This concept was introduced in 1970 by both the WHO and the American Heart Association. The concept set out detailed proposals later called stepped - care approach to the treatment

of HBP [201] set combination of drugs were introduced and addition were made to therapy when required to reduce the arterial pressure adequately. This programme served well to encourage and instruct practitioners in the treatment of HBP, and how drugs with different mechanisms of action could be usefully combined. But such formal programme of treatment are now not as popular [202]. Mere enlightened and enterprising approach is increasingly being adopted where drugs are selected with the specific needs of the patients in mind. If a drug given alone is ineffective, the present tendency is to withdraw it and replace it with an alternative, also given as monotherapy. And except a distinct need has been demonstrated, there is increasing reluctance to proceed to multiple drug. But is recognised for hydralazine but the diuretic will then be a powerful 'loop' diuretic (an ordinary thiazide will be insufficient to counter the fluid retention of minoxidil). Also beta - blocker plus prazosun plus diuretic has been shown to work well [203].

1.9.9 **Resistant Hypertension**.

When patients continue to have moderate HBP after treatment with three or more drug for at least one month, they are said to have resistant hypertension. Causes could include lack of patient compliance, inadequate drug doses, inappropriate drug combination, expansion of blood volume, use of pressor medications and presence of secondary forms of hypertension. Also excess salt and alcohol intake can cause resistance to therapy. There is also the "white coat effect" (when a patient's blood pressure only becomes elevated in the presence of a nurse or doctor). Additionally, intrinsic renal disease, side effects of drugs and expansion of blood volume secondary to blood pressure reduction can cause resistance hypertension. But the use of loop diuretic , in large doses can help to bring resistant HBP under control in some patients. The combination of ACC - Inhibitors and calcium antagonist has proved to be especially effective in severe and resistant cases.

1.9.10 **Hypertensive Emergencies**.

Conditions which require rapid reduction of blood pressure and require hospital admission with immediate intervention include severe hypertension with papilloedema or haemorrhage

in the optic fundus (malignant and accelerated hypertension), hypertension complicated by acute left ventricular failure, cerebrovascular, that the use of two agents together can minimise the side effects that one drug alone. in larger drug might impose. Further, an additional agent can eliminate an adverse effect imposed by a previous one; a typical example being the fluid retention due to methyldopa which is corrected by the introduction of a diuretic. Also few doctors now favour the use of drugs more than once or twice daily and also avoid elaborate titrations where possible. Therefore agents which can be given in one or two increaments hold a clear attraction (ensure compliance). Many doctors and patients now appreciate the rationale and simplicity of fixed drug combinations, made up in a single preparation. Likely useful twin combinations include diuretic and beta - blocker; diuretic and ACE - inhibitor (or Angiotencin II antagonist); calcium antagonist (dihydropyndia, DPH) and beta blocker; calcium antagonist and ACE - inhibitor; Alpha - blocker and beta - blocker; beta - blocker plus prazosin, beta - blocker plus ketanserin (new drug); ACE - inhibitor plus ketasenrin; diuretic plus methyldopa. Less effective combination are beta - blocker plus ACE - inhibitors and diuretic plug dihydropyndia calcium antagonist. Contraindicated combinations(similarity of action and/or danger) are methyldopa, clonidine or reserpine in any combination with each other of their central effects, ACE - inhibitor and potassium spemming diuretics, due to danger of hyperkalinia also verapamil and beta - blocker due to danger of cardiac conduction defects. But where triple combination is required, one of the best is beta - blocker, diuretic and hydralizine, ("standard triple therapy"). In resistant cases, manoxidil can be substituted in accident, acute coronary event, acute aortic dissection, hypertensive encephalophaty, hypertensive crisis of phaechromocytomes, eclampsia, and hypertension following cardiac surgery or due to a food or during interaction with a monoamine oxidase inhibitor. There are several therapeutic options for hypertensive crisis [204]. Choice depending upon the clinical situation on the doctor's experience. Drugs used include intravenous frossimide, sublingnal or intravenous infusion of nitroglycerine, or infedipine capsules chewed and swallowed. And where immediate reduction of blood pressure is necessary intravenous infusion with sodium nitroprusside, an intravenous volus or infusion of diozoxide and intravenous labetalol are

very effective. But in the hypertensive crisis of phaeochromocytoma, phentolamine should be administered [205].

1.9.11 **Anaesthesia and Treatment of Hypertension**.

In the past dry treatment of HBP was discontinued before surgery and anaethersia (to allow an intact autonomic nervous system to respond to surgical crisis such as bleeding and to avoid interaction of anesthetic drugs with antihypertensives [206]. But this is no longer acceptable some patients with uncontrolled hypertension experience more dangerous surge of arterial pressure then treated patients especially during induction of anaethesia. Also arrythoma and ischaemic ST. depression are frequent and severe in the untreated. Also the anaesthesia is able to use control of blood volume by transform to contact undue hypertension. And since any of the antihypertensives are competing that effect can be reversed, (such as beta-blocker) if necessary by increasing the dose of agonist, very large dose of catecholamines may be required. But some cardiac surgeons prefer to withdraw beta - blockade at least two days pre-operatively to reduce the risk of low cardiac output post operatively. But this carries obvious risks in those with ischaemic heart disease.

1.9.12 **FOLLOW - UP PROCEDURES.**.

Patients need to be seen at regular interval during the stabilization period of treatment, till blood pressure levels are satisfactorily controlled. During follow up doctors are expected to ensure that target DBP and SBP are reached and maintain. Also that other risk factors are controlled. Gradual and careful reduction of blood pressure will minimize side effects and complications of treatment and improve compliance sometimes "labeling" (telling a patient that he or she has hypertension may cause anxiety or mood change. Reassurance about prognosis and his or her ability to lead a normal active life is therefore particularly important. Also the need to explain any new symptom which may appear. Self assessment may ensure compliance. After stabilization, follow up visits at 3 - 6 months interval may be adequate.

And as a rule antihypertensive therapy should be maintained indefinitely. Because cessation of therapy in patients who had been correctly diagnose as having hypertension is usually followed, sooner or later, by return of blood pressure to pretreatment levels. Nevertheless, after prolonged control of blood pressure it may be possible to attempt a careful but progressive reduction in the dose or number of drugs used, especially in patients who strictly adhere to lifestyle changes, accompanied by careful, continued supervision of blood pressure[207].

1.9.13 **New Antihypertensive.**

Serotonin antagonists. Only one has so far been used in treating clinical hypertension [208]. Serotonin is a powerful peripheral vaso constrictor substance. Which can amplify vaso constrictor effects of other agents, such as angiotensin II and noradrenaline. It can cause platelet aggregation, mediated by serotonin type - 2(S_2) receptors. Ketanserin is a specific antagonist of the type - 2 receptor devoid of agonist effect. It has some alpha - blocking effect. Ketanserin lowers blood pressure possibly by affecting baroreceptor function such that a combination of powerful S_2 blockade with weaker alpha - 1 - blockade may be required for blood pressure reduction. It is given orally and gradually increase blood pressure effect over 2 - 3 months, which is greater in older patients. It has no pistinal effect and no first dose hypertension. It does not alter seron electolyte or urea but produces minor increase in serom creation. It produces dose-related group - 3 antiarrhythmic action (both volunteers and patient with hypertension) by prolonging the QT interval. When combining ketanserin with diuretic, it is prudent to include a potassium conserving agent (potassium depletion could predispose to ventricular rhythm disorders). Also it should be used with caution in atrioventricular block of group 2 or higher, or with an arrythnic agents. Other side effect include drowsiness (early treatment) than dizziness dryness of the mouth and pedal oedema.

1.9.14 **Education of Patient and Relatives**.

It is important to communicate with the patient as well as those involved in the patients care (a responsible relative in case of an elderly subject); to understand the purpose of antihypertensives, that it is preventive rather than therapeutic and life long. A common misconception that dry treatment may be stopped once the pressure has been controlled. Asking for tablets to be brought to the clinic may help identify some problems. Older patients may be forgetful and thus apply poorly. In such cases reversion to a simpler regime often improves control rather than a complex therapeutic regimen. Direct confrontation is sometimes useful; asking if tablets are "difficult" to take for some reason or enquiring about specific side - effects, (slowing of pulse rate in a patients taking a beta - blocker), may help without endangering the doctor - patient relationship. Only occasionally are patients frankly

perverse (uneaten antihypertension) drugs recovered from the locker of 16 year old with apparent due resistant hypertension who was observed to be taking tablets into her mouth then sureptiously spitting them out. Following further discussions, blood programme was controlled at 120/90mmHg from 120 - 150mmHg an atemololol 100mg plus and bendiofluezide 10mg daily.

Effective communication requires special skills such as counseling skills. Such that health workers found out about the patients in order to provide appropriate information on his or her condition and subsequent treatment. This is an important component of health care in general and care of hypertensive patients in particular. So hat patients autonomy can be respected. The implications for patient being diagnosed as hypertensive, the prognosis and the advantage of medical care need to be carefully communicated at the first meeting with the physician. The patients preferences regarding drug or non - pharmaceutical treatment can be explained at this early stage. It may help to understand the patient better and to won his or her co-operation to comply to a treatment programme. Using a combination of instruction and dialogue was fluid by the WHO to be useful "guiding the parent as ways to control his or her blood pressure and associated risk factors of present. Because compliance with a recommended therapeutic/preventive regime is a long - term, even permanent issue which requires on going educational efforts on the part of the physician or health worker.

Patient education or communication is to identify and correct patient misconception regarding hypertension (treatment is necessary only when the patient has a headache or feels dizzy). Several skills such as mnemonic technique for rewarding to take drugs, or self - measurement of blood pressure may be part of the education process.

1.10 NON PHARMACOLOGICAL TREATMENT OF HBP.

Management of HBP could be surgical, pharmacological or non - pharmacological.

1.10.1 SURGICAL THERAPY.

The surgical treatment, (not surgical correction of a specification causing secondary hypertension), of hypertension is now of history interest only. Such measures include bilateral dorsolumbar sympathetory and adrenalectory. These procedures recorded high rates of compliatus and usually unpleasant side effects. But they demonstrated the value placed

on blood pressure reduction in correcting severe complications of HBP such as malignant hypertension and hypertensive heart failure and provide a basis for the use of drug therapy.

1.10.2 **PSYCHOLOGICAL MEASURES**.

These are several non - drug methods for lowering blood pressure, including diatay lifestyle and psychological measures.

Psychological Measures. These include **Yoga, transcendental meditation, relaxation training, and biofeedback techniques**. They have been shown in the short term (with dedicated exponents) to lower high blood pressure. On present evidence, the use of such methods long term or for wide - scale therapy is more questionable but they deserve further attention.

1.10.3 **LIFESTYLE CHANGES**.

There are seven of them, four of them contribute to lowering blood pressure and three of the are for the treatment of associated risk factors. For lowering blood pressure weight reduction, reduction of alcohol intake, increase physical activity and moderation of dietary sodium are all requirement when enforced, they help to lower blood pressure, as well as avoid or reduce the need for antihypertensive drugs. These interventise have proven efficiency. Whereas stress management micro nutrient alteration and dietary supplementation with potassium, fish oil, calcium, magnesium or fibre have limited or unproved efficiency. The American Optimatic Association highlighted two issues of tremendous importance to national health, in a hypertension update. They results of systolic hypertension in the Elderly Programme, (SHEP) and the result of the trials of Hypertension Prevention, Phase Is, (TOHP-1). The results both have tremendous impact on the systematic and occular morbidity and mortality associated with hypertension,. The SHEP study indicate that stepped - treatment (initially with a low dose of chlorthaldone), of these levels, 160mmHg and above in patients 60 years and older), had a positive effect on morbidity and mortality. The short term feasibility and efficiency of modifying blood pressure by seven (7) non - pharmacological international was addressed by the TOHP - 1 repute they called it. lifestyle modification and concluded that,

the only significant blood pressure reductions were attained with modest reductions in weight and sodium intake contrary to popular beliefs and myths; reductions which translate unto decreases morbidity and mortality. Also at 1998, council for high blood pressure research, in annual conference in Philadelphia, Doctor Lindpaintner, suggested that to get blood pressure under control, the first requirement was a keep a health lifestyle in terms of some regular exercise and cease smoke.

Weight reduction. Increase body weight is closely correlated with raised blood pressure especially, where fat is accumulated on the trunk or abdomen, which is closely correlated with hypertension, hypertensive and diabetes weight reduction lowers blood pressure in the majority of hypertensive patients more than 10% overweight and beneficially affects lipid profile and insulin resistance. Structured and supervised weight - reduction through reduction of dietainy energy through undertaking regular exercise should be advised and encouraged through patient counseling and education. programmes of physical exercise should be be maintain for 3 - 6 months in mild or borderline hypertension before prescribing antihypertensive drugs. Also long - term weight reduction through difficult to maintain is a lifestyle modification goal. Three large controlled trials have demonstrated the effected weight loss on the primary prevention of HBP. In the TOHP - 1 study of non drug interventions in people with high to normal blood pressure, mean weight losbles in men were 4.7kg and 1.6kg for women at 18 months with corresponding means SBP/DBP reduction of 3.2/2.8 mmHg in men and 2.0/1.1 mmHg in women. Also, since obesity is associated with abdnormailities in seronlipids and insulin and glucose metabolism reinforce the value of the control of obesity as a lifestyle intervention for blood pressure reduction.

Reduction of Alcohol intake. Where alcohol intake is regular in both men and women of different ethnic groups as a habit, there is prevalence of HBP. But reduction of alcohol intake over a period of 1 - 4 weeks results in lowering of blood pressure when alcohol intakes is in moderation while reducing excess weigh; there is cumulative effect in reducing overall cardiovascular risks. Randomised cross-over studies showed that reducing alcohol intake by

80 - 85% resulted in a reduction of 5/3mmHg of blood pressure, in hypertensive subjects and 3.8/1.4 mmHg in those with normal blood pressure. Under randomised factorional study showed that restricted alcohol intake alone resulted in a reduction of 4.8/3.3mmHg SBP/DBP, while combined alcohol and energy restrictions resulted in an average reduction of 10.2/7.5mmHg and a weight loss of 10kg.

Increased physical activities. Regular graduated exercise may be beneficial for both prevention and treatment of hypertension. Sedentary and unfit normotensives have a 20 - 50% higher risk of development HBP than those who are more active. Researcher also found that exercise is safe for women with a history or miscarriage and early birth. They also reported that exercise did not increase the risk of pregnancy - induced hypertension or aggravated chronic hypertension. Also, several studies have shown that exercise may be a prescription for women with diabetes. The experts also advised common sense; not too much too fast and increase culvert in take (to take cues from the body). And they recommend that exercise which require balance should be avoided as a fall could be dangerous for the mother and baby.

Exercise has also been found to lower systolic and diastolic blood pressure by 50 - 10mmHg dynamic **isotonic exercise** such as walking is said to be more effective than static **isosmotic exercise** such as weight lifting. Milder levels of exercise, such as brisk walking for 30 - 60 mmHg a day or 3 - 5 trues a week, is said to be possibly better than more strenuous from of exercise such as running. And according to Gibson, several anecdotal and controlled studies have confirmed that blood pressure is lowered acutely by exercise. This effect is said to be substantial, about 10 - 12 mmHg and lasts for a few hours. And from studies of more prolonged exercise it was found that increased physical fitness, (such as obtained by 20 - 30 minutes of moderate exercise 4 - 5 times a week), is accompanied by significant lowering of blood pressure, by a bit 7 - 10mmHg. The beneficial effects of exercise, may be modest but they are useful in lowering blood pressure for purposes of prevention as well as control. This conclusion was reached after analysis of 22 studies (of which 10 included normolysive subjects). These studies revealed that if stitches are methodologically adequate, a mean

reduction in SBP of 6.4 mmhg and DBP of 6.9mmHg as achieved through prescribed exercise (a,b). And another analysis of 30 randomised controlled trail of **lower extremity aerobic exercise** revealed a 3mmHg reduction in SBP and DBP.

Reduced Salt Intake. Both studies involving eyndemiological observation and clinical trials show an association between diatany sodium intake and blood pressure (a,b). Individuals vary greatly in the response to changes in dietary sodium chloride Black and elderly people may be more sensitive to salt reduction. An average intake of 6g of. sodium chloride a day should be the aim. Meta - analysis of 18 channel trials in hypertensive subjects revealed a blood pressure reduction of 4.9 mmhg SBP and 2.6 mmhg SBP in 1 - 2 months. This was associated with a 56 - 105 mol. reduction in daily sodium intake. A larger analysis of 78 trials of sodium restriction, are quarter of which included harmotensive subjects, demonstrated that observed and predicted blood pressure reductions were most similar in trials lasting over five weeks. suggesting that effects of sodium restriction may take several weeks to become evident.

Lifestyle measures for the treatment of associated risk factors. These include cessation to tobacco smoking, reduced fat intake and control of diabetes.

Cessation of tobacco smoking. Although tobacco smoking is not causally related to HBP, it is a major cardiovascular risk factor. The incidence of stroke and coronary heart disease in hypertensive patients who smoke is 2 - 3 times greater than in non - smoking patients with comparable blood pressure. Stopping smoking rapidly reduces this risk. Therefore persuading hypertensive patients not to smoke is the most effective single way a physician can reduce their risk. Smoking control should also be an intergral part of any programme for primary prevention of cardiovascular disease in populations.

Reduced fat intake. Higher serum cholesterol high-density lipoprotein – cholesterol level and low serum high density – lipoprotein cholesterol levels increase the risk of atherosclerotic complications of hypertension although there is some undertainty whether this is true above the age of 70 years. So, nutritional counseling and drug treatment as appropriate are indicated to control these risk factors.

Hypertriglyceridaemia. Is a much debated cardiovascular risk factor which is frequently associated with insulin – dependent and non – Insulin – dependent diabetes mellitus and insulin resistance. But increased physical activity and nutritional counseling are both recommended for treating hypertriglyceridaemia. Since increased physical activity is also likely to reduce body weight and blood pressure, it is appropriate in hypertensive with

hyperpidaemia as well as disturbed glucose metabolsim. Advise an nutrition and physical activity is an essential part of a primary prevention programme that aims to reduce the total risk of cardiovascular disease [228]

Control of diabetes. Diabetes requires a comprehensive plan of care which includes specific nutritional counseling and appropriate use of insulin and orally active hypoglycemia drugs (229). According to Fieldsman and Bierbrier insulin resistance is associated with HBP (230). Although it is not know if this relationship is causal. Studies have shown that insulin increases skeletal muscle blood flow despite increasing sympathetic activity. These workers also studied insulin – mediated alterations in dorsal – hand – vein compliance in normotensive and mild and borderline hypertensive, in order to determine if insulin may act as a direct vasodilator or if insulin – mediated vascular effects are altered in hypertension. Their results showed that insulin caused a dose – dependent increase in venous dispensability in phenylephrine pre – contricted vessels. But insulin – mediated venodilation was significantly impaired in hypertensive. Also, the vasodilator potency of insulin was significantly correlated with both blood pressure and body mass index. Insulin they suggested may be an endogenous vasodilator. And further, that in hypertensive and obese patients impairment of insulin mediated vasodilation may contribute to the increase in peripheral resistance characteristic of HBP. According to the WHO, several life-style measures, such as regular exercise, moderate weight reduction and a low fat, high – carbohydrate, high – fibre diet, can improve insulin sensitivity and may help reduce the contribution of insulin resistance to increasing blood pressure. Several clinical trials of life-style changes showed reduction in severity hypertension; the primary prevention of hypertension study by 54%. The hypertension prevention of hypertension trial by [231] 20 – 35% and by 51% with weight loss and 24% with sodium reduction in the trials of hypertension prevention [232].

1.11 AIMS AND OBJECTIVES

1.11.1 AIMS OF THE STUDY

The aim of this study was to determine whether the therapeutic protocol of hypertension conforms to global standards by using the patient approach. This approach involved the use

of patient medical records in conjunction with patient interview, for the period of the study (November 1997 to November 1998).

1.11.2 OBJECTIVE OF THE STUDY

The objectives of this study included the determination of **prescriber preferences, patient perception and satisfaction with their treatment**; with a view to identifying the drugs which are prescribed. This information will enable the ABUTH Management to provide the Pharmacy with adequate levels of the drugs required for the treatment of hypertension.

1.11.3 Relevant Research Questions.

These include **personal data** – what is patient Age, Sex, Weight, height and Occupation? **Patient family history** – is either of the parents hypertensive? **Social history** – is patient a smoker? Does patient consume alcohol or chew kolanut? Does patient add table salt to food? Does patient consume potash (Hause "kanwa", Yoruba "kaun")?

Patient Clinical history – what is patient age at diagnosis? Does patient have any other illness? What was patients' presenting complaint? Was it stroke? Headache? Cardiac failure? Was hypertension pregnancy-related? If so, was it pregnancy aggravated hypertension, PAH, or pregnancy induced hypertension (PIH)?

Patient drug history – Are drugs prescribed easily available? Have prescriptions been changed? How many times? For what reasons? Do patients initiate the change (i.e. undesirable side effects or adverse drug reactions) or do prescribers initiate the change (i.e poor control, non-complaint patient etc).

Non-drug therapy - Has doctor advised exercise? Has doctor prescribed diet?

1.11.4 Delimitation Of The Study

In this research, presenting complaints, social and family history, clinical and drug histories as well as non-drug therapy were used to study the therapeutic protocol of hypertension at ABUTH Zaria between November 1997 and November 1998.

1.11.5 Significance Of The Research Problem And The Justification For Studying It.

High blood pressure is a very common condition and an important public health problem in all countries of the world. This is because, if hypertension is untreated, the risk of

complications increase and the life expectancy of the patient decreases [14]. Therefore, good control, management and treatment, as promoted by the WHO is required. A necessary step towards achieving this is the study of the therapeutic protocol of hypertension in the chosen institution.

CHAPTER TWO

METHODOLOGY.

2.1 BRIEF OUTLINE OF THE RESEARCH PROCEDURE

The WHO in 1996[233] proposed two complimentary approaches to control hypertension. The public health or population approach, and the clinical or individual approach.

2.1.1. POPULATION APPROACH

The goals of the population approach includes enhancing public awareness to the fact that high blood pressure is a major health problem and may indeed be "a silent killer". Efforts should be geared towards detecting individuals with high blood pressure or those at risk of developing it and advocating lifestyle changes which minimise or eliminate the controllable risk factors of hypertension. These goals can be achieved through public education, appropriate training of health professionals as well as adequate enlightenment of patients with hypertension.

The Public

The public which usually culturally, economically, environmentally and geographically diverse, requires a combination of methods for effective delivery of messages. These include announcements via radio, handbills, television, posters, community centres, work sites, schools and religious centres. This approach has been successful in Canada, Finland and the United States. [233]

The Health Professionals

These include doctors, pharmacists, nurses and others. They all require appropriate training in detection, management and prevention of hypertension. This can be achieved through emphasis on curriculum, re-training and certification, to enable them be successful counselors and advocates of healthier lifestyle in their community.

The Patient

Hypertensive patients need to be educated on their health condition, its consequences and the need for effective management and the benefits of changing their lifestyle. These include compliance with health care advice, regular monitoring and regular visits to the clinic to discuss the effects of treatment with health providers, and enlisting family members in the adherence to health care advice.

2.1.2 THE INDIVIDUAL APPROACH

Many people with hypertension may not benefit from the population approach. So, there is need to develop an individual approach which involves the use of non-pharmacological intervention as an adjunct to drug therapy.

This approach also differs from country to country and consists of;

Health education for the whole community including children.

Agricultural Polices which ensure that potassium - rich natural foods, (fresh fruit, vegetables, etc), are inexpensive and readily available.

Food industry Policies to regulate and promote availability of low-salt and low fat food items and to label such items with their salt and fat content.

Recreational Facilities - Provision of such facilities for outdoor sports and leisure time.

Tobacco Policy - To control tobacco smoking especially in public places, tobacco being an important additional risk factor for cardiovascular disease.

Drug Policy - Availability of inexpensive but effective drugs for lowering blood pressure.

Health Care Policy - Integration of blood pressure detection, treatment and control into the three tiers of health care especially the primary health care.

2.1.3 THE RESEARCH APPROACH

The World Health Organisation recommends that each country develop database for epidemiological programme and evaluation research and implementation of population - based hypertension control programmes.

Epidemiological Research - involves data - collection on prevalence of blood pressure in different sectors of the population, frequency of the various factors which contribute to the

risk of developing hypertension, and the frequency of other cardiovascular risk factors which contribute to hypertension.

Programme Research - This involves development and implementation of programmes relevant to each tier of the health care delivery relevant to each community.

Evaluation Research - This entails continuing monitoring, evaluation and maintenance of the cost-effectiveness of intervention programmes.

Implementation - The WHO has recommended National programmes for the control of hypertension in countries where hypertension has been identified as a major health problem or is increasing with changes in lifestyle. This could be achieved by raising awareness, advising and educating the community and individuals, ensuring active community participation and creation of the environmental conditions that support healthy diets and healthy social behaviour patterns.

2.1.4 THE HYPERTENSION - MANAGEMENT AUDIT

In the World Health Organisation hypertension Management Audit for Europe and the World, a five - step approach was used to evaluate hypertension control in populations. The **"Population approach"** - This involved a classical epidemiological survey of a random sample of a population, for the assessment of basic indicators of awareness of hypertension in the community, such as the proportion of undiagnosed and untreated, as well as over diagnosed and possibly unnecessarily treated, (those who can be managed with diets and exercise alone), hypertensive patients.

The **"Patient approach"** - In this case, a sample of patients with established hypertension is to be selected and their case histories were reviewed. This patients survey was a medical audit - a retrospective assessment of the quality of care on the basis of medical records. The WHO/ISH (International society of hypertension) guidelines for the management of mild hypertension were selected as the standard of adequate treatment, for comparison.

The **"Consumer approach"** - In this case, patients are to be considered as the consumers of medical care. Their perceptions and satisfaction were taken as important indicators of

certain aspects of the complex process of hypertension control. The consumer inquiry was an attempt to assess the clients mood, their readiness to follow advise and their possible complaints about the care received.

The "**Physician approach**" - Here, the inquiry is to be used to assess the knowledge and attitudes of physicians involved in the control of hypertension. For this purpose a questionnaire is to be administered to a sample of general practitioners and specialists in internal medicine. The responses will be limited to knowledge and attitudes. These were not likely to have measured what physicians were in fact doing but rather described what they thought they ought to do. Still, these "Self portraits" were found to be valuable in the sense that actual behaviour is unlikely to be better than the ideas and intention of the respondents.

The "**Drug utilisation approach**" - Here established methods are to be quantitatively used to assess the amount of antihypertensive drugs prescribed in defined daily doses, related to the number of inhabitants of a community and the prevalence of hypertension. It also assessed the pattern of drug utilisation. Both the amount and structure of utilisation were found to be valuable health care indices, complimentary to information received from epidemiologic and clinical approaches.

These five - step approach to evaluation produced relevant indication of the quality of antihypertensive management.

2.2 RESEARCH QUESTIONS

The decision criteria which were used include personal data, family history, social history, clinical history, drug history and non - drug therapy. These are decision - criteria by which the protocol for hypertension management in ABU Teaching Hospital Zaria, was evaluated.

2.3 RESEARCH DESIGN

Both questionnaire survey and the retrospective survey of patient case histories were used for data collection.

2.4 RESPONDENT CHARACTERISTICS AND CLASSIFICATION

Data was collected from a sample of out-patients, with established hypertension attending the cardiac clinic of ABU Teaching Hospital, Zaria for management of their hypertension.

2.5 DATA COLLECTION

The questionnaires were administered to the patients, waiting to consult their doctor, at the cardiac clinic. And subsequently, their case folders were retrieved from the medical records office in order to complete the retrospective portion of the questionnaires Out of 100 questionnaires that were administered, a total of 41 questionnaires were duly completed.

2.6 DATA PROCESSING

A spreadsheet was prepared from the completed questionnaires (Appendix 1). Then, a frequency count was used to record responses for each criterion. These results were then tabulated from the tables, bar charts and pie charts were constructed, as applicable.

Mean values and percentages and standard deviations were also calculated where applicable.

And the confidence interval of 99 percent was constructed for the results where applicable.

The results have been presented in 4 bar charts and 13 pie charts.

Personal Data are presented in tables A. 1, A.2, A.3 and A.4 with bar charts for A.1 and A.2, representing Age and Sex distribution of data, respectively. Pie Chart for A.4.

Family History is presented in tables B.1, B.2, B.3 and B.4 and one bar chart for B.2 representing number of pregnancies, for female patients. Pie Chart for B.1,B.2,B.3,B.4.

Social History results are presented in tables C.1, C.2, C.3, C.4, C.5, C.6, with a bar chart for C.3, representing number of cigarettes smoked per day. Pie Chart for C.1, C.2, C.3, C.4, C.5, C.6,

Clinical History is presented in tables D.1, D.2 and D.3 with one bar chart for D.1 representing patient age at diagnosis. Pie Chart for D.2.

Drug History is presented in tables E.1, E.2 and E.3. Pie Chart for E.2 and E.4 Finally, non-drug therapy returns were presented in tables F.1 and F.2 as pie charts.

2.7 LIMITATIONS TO THE QUESTIONNAIRE SURVEY

Newly diagnosed hypertensive patients were not included in the survey as they have no prior records to allow for the retrospective study. Also, only known hypertensive cases who attended the clinic for the period of the survey, (November, 1997 to November, 1998), were included in the survey. This was necessary to allow for relevant information to be obtained using the administered questionnaires.

Many female respondents objected to questions on their social history especially intake of tobacco and alcohol. Because they considered such social habits to be associated with "Women of easy virtue" but not with "respectable or married women "such as themselves.

But the purpose of the question was to create patient awareness that alcohol and tobacco are additional risk factors to the development of hypertension. And a knowledge of their infertile was important to the successful management of their condition. Also, there was

reluctance to divulge information on family history (the hypertensive parent). But after explanation on the relationship of parental hypertension to its later development in offspring, respondents provided relevant responses, to the two "objectionable" questions.

CHAPTER THREE

DATA PRESENTATION AND ANALYSIS

3.1 INTRODUCTION

The collated data were analysed according to the criterion group returns and according to the research questions.

3.2 CRITERION GROUP RETURNS

Responses were received from 41 respondents who have been attending cardiac clinic, of ABU Teaching Hospital Zaria, for HBP. These respondents were those who attended the clinic during the period of the survey from November, 1997 to November, 1998.

3.3 PRESENTATION AND DATA ANALYSIS ACCORDING TO RESEARCH QUESTIONS

Personal Data survey of patients revealed that females out numbered males (31 females, 10 males) at this cardiac clinic. Hypertension was found to mostly afflict females of 41 to 60 years and males of 50 - 70 years of age. About one third (31 %) of patients (males and females) were obese. Female patients were mostly housewives (36%) and petty traders (36%) but male patients had varied occupations.

Family History survey showed that 29 patients (71%) had no parental history of hypertension. Of the remaining patients (15%) had hypertensive fathers also, 15% had hypertensive mothers. Non of the patient had both parents suffering from hypertention in non of the patients were both parents hypertensive.

In most females, the hypertension was pregnancy-associated where 43% of case were pregnancy - induced while 17% were pregnancy - aggravated.

Social History revealed that few patients consumed alcohol (7%), smoked cigarettes (17%) while many patients consumed kolanut (71%), added salt to their food (56%), and consumed potash in their food (88%).

Clinical history survey showed that the average age at **diagnosis** was between 20 and 70years for females and 30 and 60years for males, (co-existing illness), was (34%). **Presenting complaints** mostly involved he nervous system (46%), the cardiovascular (20%) and the respiratory system (12%).

Drug History of the patients showed that **Diuretics** was most frequently prescribed (41%) and (34%) of patients had their prescriptions changed at least twice, during the period of the survey. The change in prescription was mainly due to poor blood pressure control (33%) incidence of side - effects (26%) and poor compliance (19%). The survey of the current patient prescription, at the time of the survey, revealed that diuretics are the most readily prescribed (29%), followed by beta - adrenoceptor blockers (17%), while calcium antagonist, ACE - Inhibitors, are prescribed at appreciable frequency and acetylsalicylic acid (aspirin) is increasingly being prescribed.

Non-Drug Therapy Such as physical exercise and diet were rarely recommended (15%) while on the contrary salt restriction was frequently (88%) advocated.

3.3.1 PERSONAL DATA ANALYSIS

The incidence of hypertension in females occurred between 20 - 80 years, the highest incidence being from 40 - 60 years. For the male patients it ranged from 30 - 80 years. The highest incidence was from 60 - 70 years. The mean age for both male and female was 48.26 years, standard deviation 13.28, confidence interval of 99% [43, 54] (Table A.1). The **body mass index** (BMI) was computed using patient weight and height measurements (Tables A.2 and A.3) BMI, ranged from 15 - 30 and above. (15%) of patients were underweight with BMI below 20. (24%) had desirable weight with BMI of 20 - 24.9 and (24%) were overweight (25-29.9) and many patients were obese, BMI of 30 and above (37%).

Occupational Distribution of the patients showed that the females were mostly housewives 36.5% and petty traders (41.5%).

3.3.2 FAMILY HISTORY ANALYSIS

Family history of hypertension was low (30%). Fathers and mothers were equally afflicted with hypertension (15%) each. But the majority (70%) had no **parental** history of hypertension (table B.1). Incidence of hypertension among other first degree relatives (siblings) could not be investigated in this study, because information concerning brothers or sisters of patients not available in the medical record of the patients.

The number of pregnancies most associated with hypertension, in this study was 6 - 10 pregnancies (mean pregnancy 8, standard deviation 3.6) (Table B.2).

The incidence of PIH was established whenever the female patient admitted no hypertension in previous pregnancies and when after delivery of the baby during whose pregnancy, they were found to have hypertension, their blood pressure did not return to normal or pre-pregnancy levels. and they had since been attending the cardiac clinic for management of their blood pressure.

3.3.3 SOCIAL HISTORY ANALYSIS

Six criteria were used to evaluate patient social history and these include (alcohol consumption, cigarette smoking, cola-nut use, salt intake, and potasium consumption).

Cigarette - smoking - was more among females (5 out of 7 are smokers) and they had been smoking between half - a - stick to 14 sticks per day, (as adolescence) prior to being diagnosed as having hypertension whereas only 2 male ex-smokers were in the survey. And they smoked between 3.5 - 28 sticks per day.

Kolanut - Use was also high (70%). In this geo-political area, kolanut is used as a stimulant substance. Studies which can be correlated with this findings were based on caffeine consumed through drinking coffee.

Salt intake was high (56%) as many patients had formed the habit of adding salt to their meals, at table.

Potassium carbonate (K_2C0_3), **potash** is commonly added to meals while cooking in this environment, as revealed in this study.

3.3.4 CLINICAL HISTORY ANALYSIS

Three criteria were used to evaluate aspect of clinical history of patients namely,

Age at Diagnosis was 20 - 50 years for females and 30 - 60 years for males. The mean age at diagnosis was 43.28 years.

Co-existing illness (such as diabettes, renal failure) had an incidence of (34%.). The major presenting complaint affected mainly the **Peripheral** and **central nervous system** (46%) with symptoms such as (headache, parenthesis, dizziness, fainting, unconsciousness and high blood pressure).

The **Cardiovascular system**: shortness of breath, (SOB), dyspnea on exertion, (DOE), paroxysmal nocturnal dyspnea, (PND), rheumatic heart disease, post - partum cardiac failure (PPCF), and palpitations, **Respiratory symptoms** 12% (cough, chest pain, epigastric pain, choking and epistaxis). Other organs were affected to a leaser extent, Ophthalmic 6% Endocrine/reproductive 2% i.e. contraceptive use, Gastrointestinal 2%, musculosceletal 8% (Table D.3).

3.3.5 DRUG HISTORY ANALYSIS

The type of prescription (at diagnosis and current at the time of the study), the frequency at which prescriptions were changed, the reason for prescription change and desire for change in current prescription were investigated.

At diagnosis, apart from anti-hypertensive, other agents prescribed as adjunct to management of hypertension or as treatment for co-existing illnesses include, **anxiolytics** such as bromazepan, diazepan (4.7%), Digoxin (7%) for congestive heart failure e.g PPCF, drugs for peptic **ulcer** disease, magnesium trisilicate (1.2%), Ranitidine (1.2%). In the antihypertensive class, **diuretics** (41.%) were mostly prescribed followed by centrally - acting drugs (17%o) others with low prescriptions levels were **calcium antagonist** (8%), ACE - inhibitors (3.5%) beta - adrenoceptor blockers (2.3%) adrenergic receptor blockers (1.2%) and Acetazolamide (1.2%) for reducing intra-ocular pressure.

< Prescription change was (83%) and ranged from only once (22%) to those patients whose prescriptions were changed more than four times as at the time of the survey (10%).

The reason for prescription change ranged from side effects (26%) lack of blood pressure control (33%) poor compliance (19%) and cost of the drugs (12%).

Subsequent prescription (during the period of the survey) showed that diuretics were the leading drugs (29%) then bete - blockers (17%), calcium antagonists (12%) followed by ACE - inhibitors methyldopa and Aspirin.

The desire for change in current therapy was low (15%). Only 6 patients mostly male (67%>) i.e. four male and two female patients, for varied reasons. The reason ranged from **erectile impotence,** to **fatigue (on methyldopa), Nausea** (on slow-k, a **potassium supplement).** Literature have documented the incidence of nausea for slow K and somnolence or fatigue for methyldopa[256] (table E.4).

4.3.6 NON DRUG THERAPY ANALYSIS

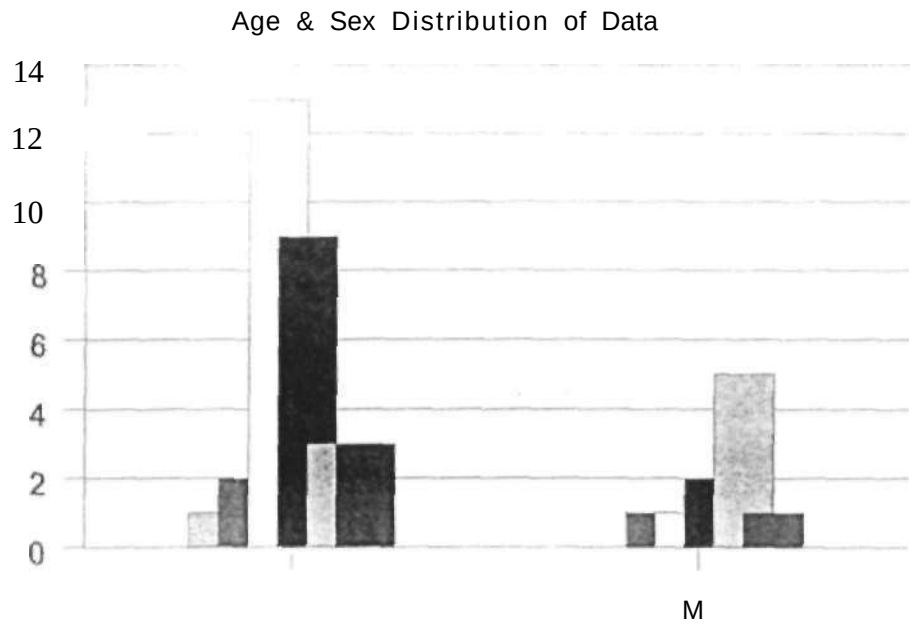
Physical exercise was rarely recommended (15%)) and the only dietary recommendation which was emphatic i.e. salt restriction (88%).

Table A: PERSONAL DATA

Al Age and Sex Distribution hypertensives.

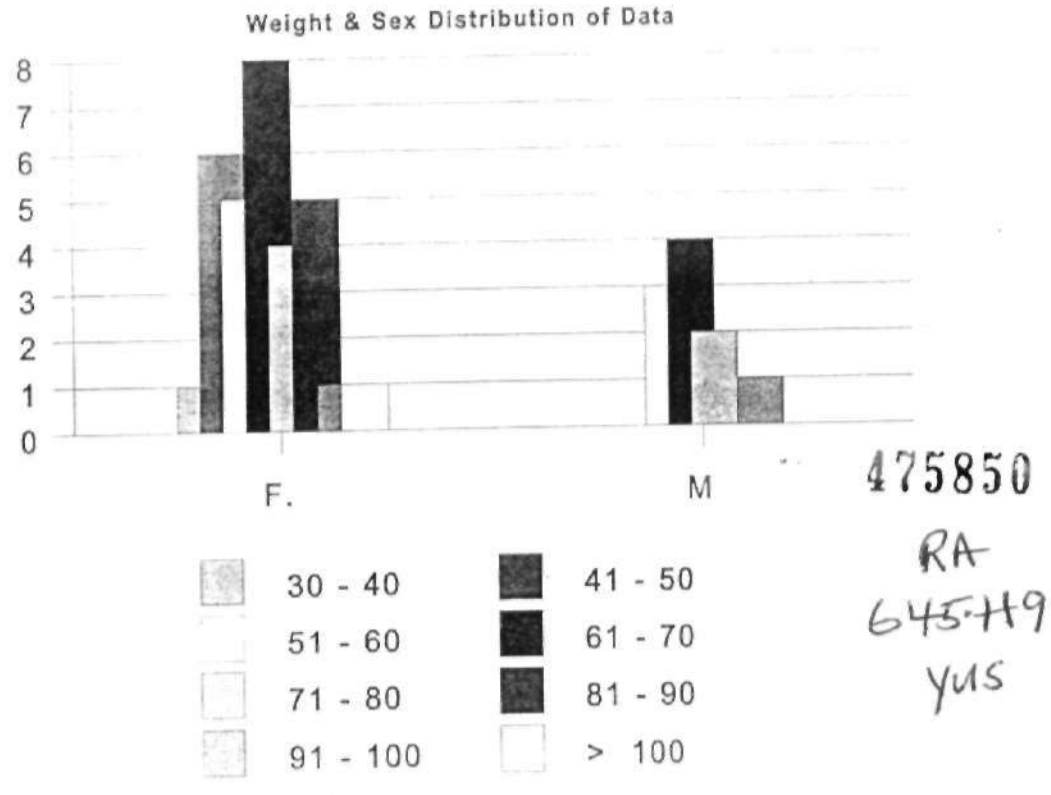
Age (years)	F	**M**	Frequency
20 - 30	1	-	1
31-40	2	1	3
41 -50	13	1	14
51-60	9	2	11
61 -70	3	5	8
71 -80	3	1	4
			41

Confidence intervals (99%) (43, 54) mean _48.26 Standard deviation 13.28.



A.2 **Body Weight Distribution amongst hypertensives**

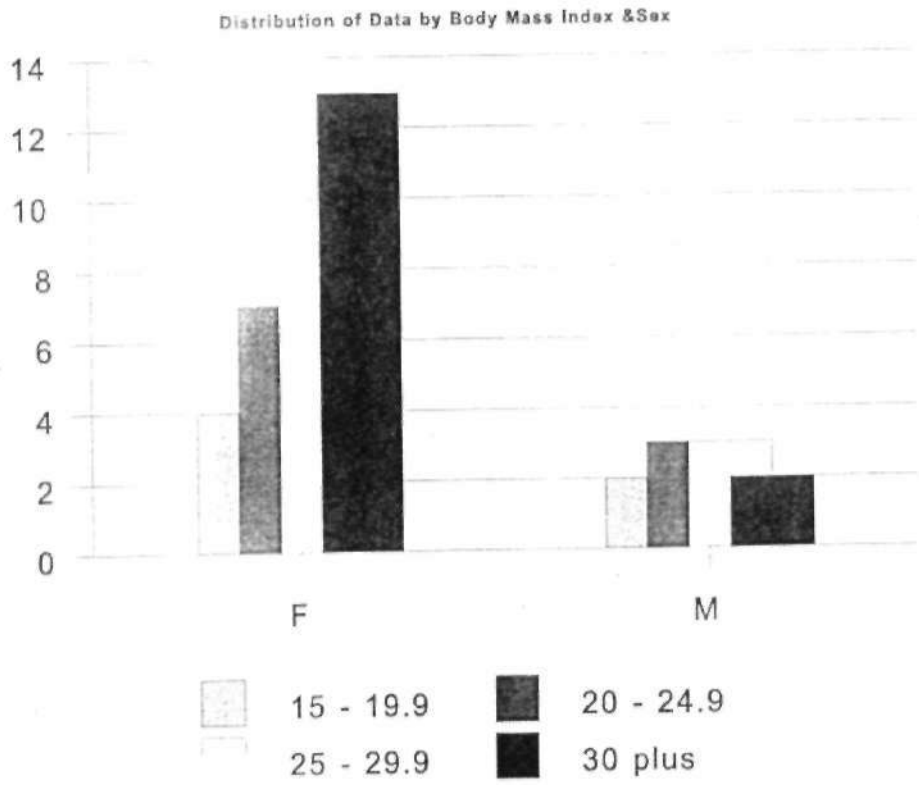
Weight (kg)	F.	M	Frequency
30 – 40	1	-	1
41 – 50	6	-	6
51 – 60	5	3	8
61 – 70	8	4	12
71 – 80	4	2	6
81 – 90	5	-	5
91 - 100	1	1	2
> 100	1	-	1



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A. 3. **BMI Distribution amongst hypertensives**

BMI	F	M	Freq.	%
15 - 19.9	4	2	6	15%
20 - 24.9	7	3	10	24
25 - 29.9	7	3	10	24
30 plus	13	2	15	37
			41	100%



A. 4 **Types of occupations in a population of hypertensives**

Type of Job	F	M	Freq.	%
Trader	15	2	17	41.5
House Wife	15	-	15	36.5
Teacher	-	2	2	5
Tailor	1	1	2	5
Civil Servant	-	1	1	2.4
Farmer	-	1	1	2.4
Laundry/Washman	-	1	1	2.4
Plumber	-	1	1	2.4
Welder	-	1	1	2.4
			41	100%

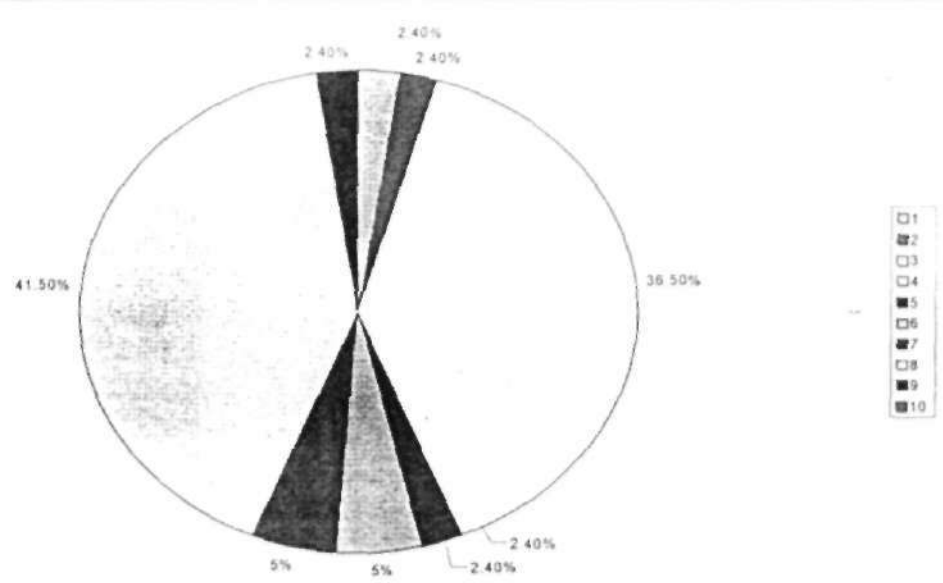
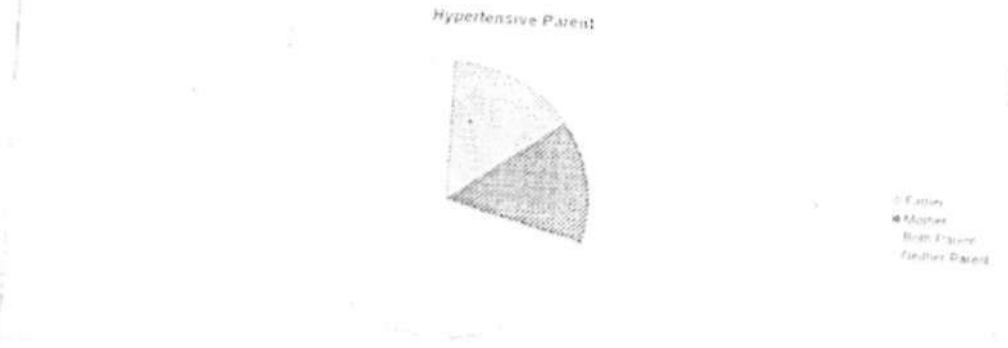


TABLE B: FAMILY HISTORY

B.1 hypertensive Parent

Response	Father	Mother	Both Parent	Neither Parent	Total
Frequency	6	6	0	29	41
%	14.63	14.63	0	70.73	99.99



B. 2 NUMBER OF PREGNANCIES: **FEMALE PATIENTS ONLY**

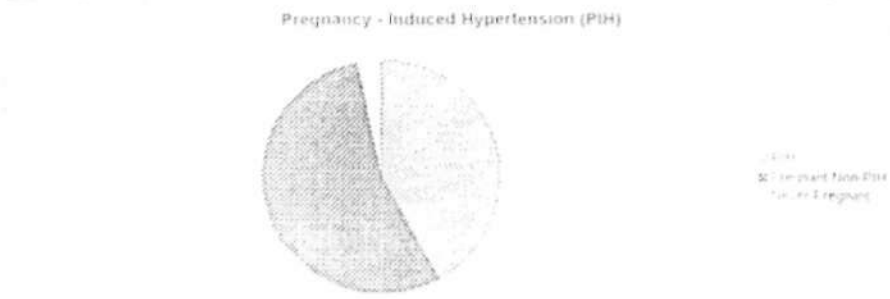
Number of Pregnancy	*Frequency*	Mean	S.D
0	1		
1 – 5	7		
6 – 10	15		
11 – 15	8		
	31		

Confidence level 99%. ( )



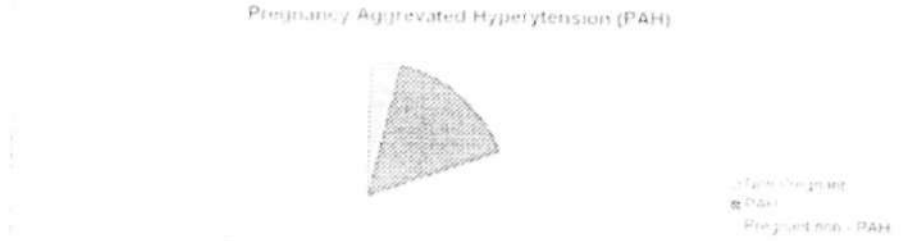
B. 3 Pregnancy - Induced Hypertension (PIH).

	Frequency	%
PIH	13	41.93
Pregnant Non-PIH	17	54.83
Never Pregnant	1	3.23
	31	**99.99**



B. 4 **Pregnancy Aggrevated Hypertension, PAH**

	Frequency	**%**
Non Pregnant	1	3.00
PAH	5	16.00
Pregnant non – PAH	25	81.00
	31	**100**



C. SOCIAL HISTORY

C. 1 Alcohol Intake

	Frequency	%
Take Alcohol	3	7
Tee Total	38	93
	41	100%



C. 2 Cigarette Smoking

	Frequency	%
Smoker	7	17%
Non-Smoker	34	83
Total	41	100



C. 3 Number of cigarettes Smoked per day distributed by sex.

SEX

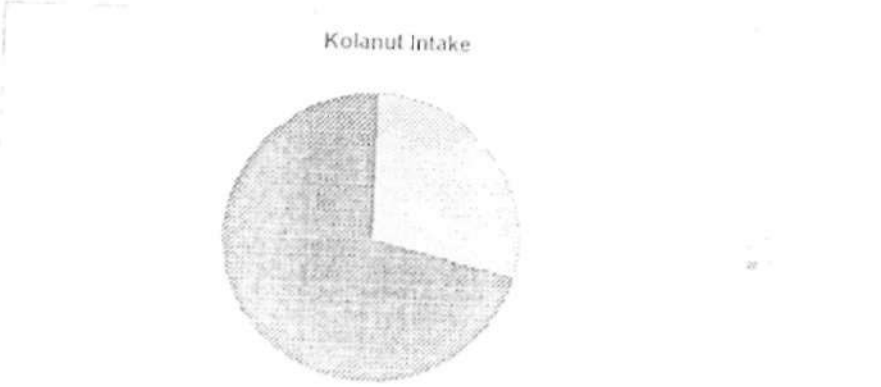
Number of Sticks	M	F	Frequency	%
0.5 – 5	1	4	5	
6 – 14	1	0	1	
15 – 28	0	1	1	

Confidence Level (99%) (-0.52, 13) Mean = 6.46 S.D. =7.16.



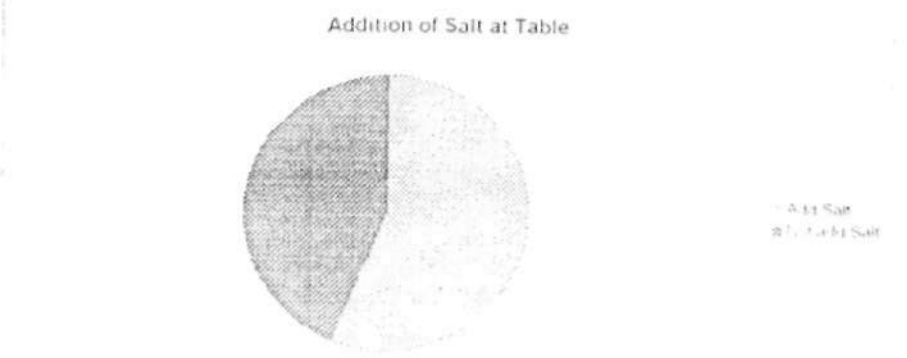
C. 4 Kolanut Intake

	Frequency	%
Take Kolanut	29	71
Not take Kolanut	12	29
	41	**100%**



C. 5 Addition of Salt at Table

	Frequency	%
Add Salt	23	56
Not add Salt	18	44
	41	**100**



C. 6 Potash Intake

	Frequency	%
Take Potash	36	88
Not take Potash	5	12
	41	**100**

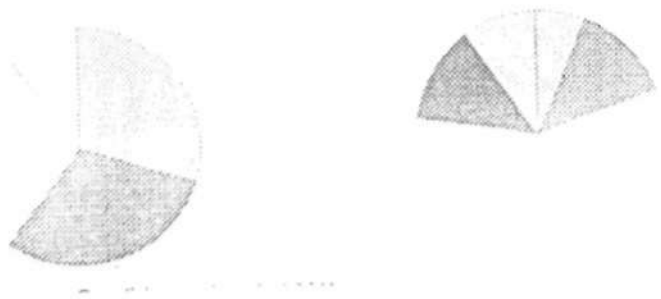


1) **CLINICAL HISTORY**

D. 1 Age at Diagnosis: Distributed by Sex

SEX

Age in means	F	M	Freq.	%
10 – 20	2	-	2	5
21 – 30	4	-	4	10
31 – 40	7	3	10	24
41 – 50	11	3	14	34
51 – 60	4	3	7	17
61 –70	3	1	4	10
			41	100



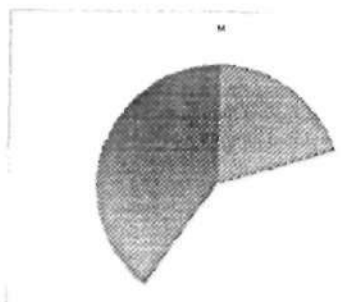
Confidence level (99%)

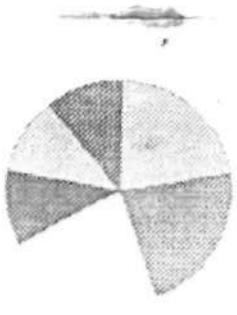
26.8, 59.8) _ 43.28 δ 12.8. (S.d.)

D. 2 Co-existing illness, distributed by Sex.

Type of illness	F	M	Freq.	%
ANXIETY	-	1	1	7
CCF	2	2	4	29
OA	2	-	2	14
OPHTHALMIC	1	2	3	21
PUD	1	-	1	7
RHD	1	-	1	7
STROKE	1	-	1	7
TB	1	-	1	7
			41	100

	Frequency	%
Other Illness	14	34
No other Illness	27	66
	41	100

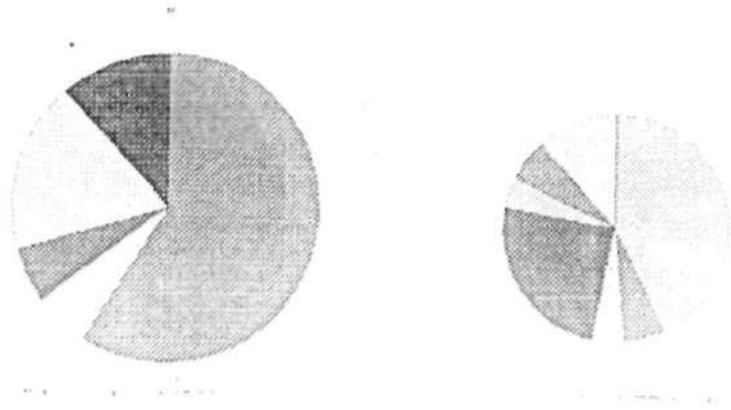




D. 3 Presenting Complaints: Distributed by Sex

Target Organ/System	F	M	Freq.	%
CNS/PERIPH. NERVOUS SYSTEM	29	10	39	46.0
The EYE/OPHTHALMIC	4	1	5	6.0
ENDOCRINE/PEPROD.	2	-	2	2.0
GASTRO-INTESTINAL (GIT)	1	1	2	2.0
THE HEART/CVS	17	-	1	20.0
THE KIDNEY	3	-	3	4.0
MUSCULO-SKELETAL	4	3	7	8.0
RESPIRATORY	8	2	10	12.0
			85	100

Confidence level (99%) (3.3, 17.9) 10.63 ± δ 10.63, 8 11.72.(S.d.)



E. **DRUG HISTORY**

E.1. **Prescription: At Diagnosis.**

Drug Class	F	M	Freq.	%
DIURETIC	**27**	**8**	**35**	**41.0**
CNS ACTING ANTI HYPERTENSION	**11**	**4**	**15**	**17.0**
CALCIUM CHANNEL BLOCKERS (CCB)	**4**	**3**	7	**8.1**
POTASSIUM CHLORIDE (SLOW K) MIST POT CIT	7	-	7	8.1
DIGOXIN	6	-	6	7.0
ANXIOLYTIC	4	-	4	4.7
ACE INHIBITOR	2	1	3	3.5
VASODILATORS	-	2	2	2.3
BETA –ADRENOCEPTOR BLOCKERS	2	-	2	2.3
ACCETAZOLAMIDE	1	-	1	1.2
ADRENERGIC RECEPTOR BLOCKERS	1	-	1	1.2
VISKALDIX	-	1	1	1.2
			86	

MIST. MAG. TRISILICATE	1	_	1	1.2
RANITIDINE	1	_	1	1.2

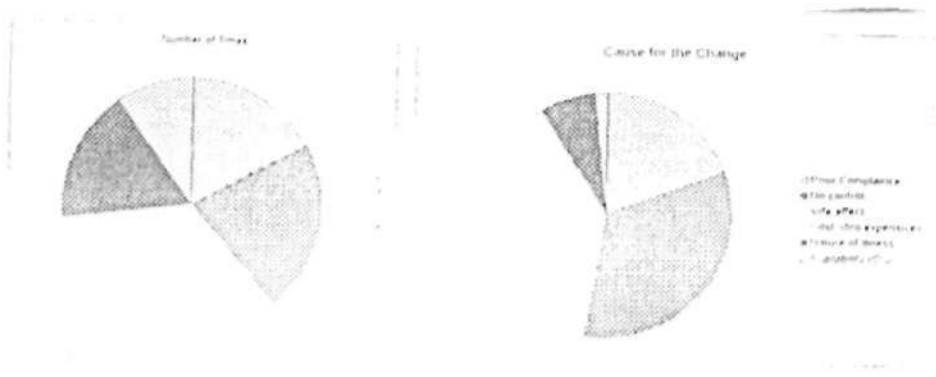
Confidence internal (99%)

(-3.5, 15.8) _ 6.14 S.d. 8.84

E. 2 **Change in Prescription Frequency and cause of change**

Number of Times	Freq.	%		Cause for the change	Freq.	%
None	7	17.0		Poor Compliance	11	19.3
1	9	22.0		No control	19	33.3
				Side effect	15	26.3
2	14	34.0	83%	Cost (too expensive)	7	7.0
3	7	17.0		Nature of Illness	4	1.8
4	4	10.0		Availability (O/S)	1	100
	41	**100**			**57**	**1.8**

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E. 3 Current Presentation: Distributed by Sex.

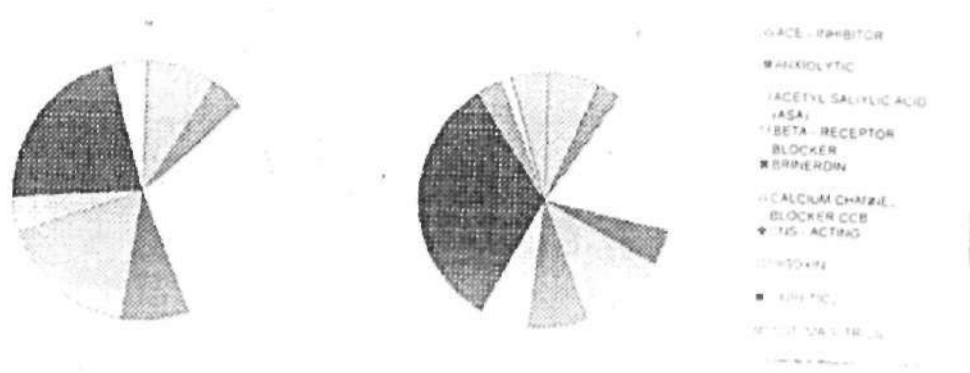
Drug Class	F	M	Total	%
DIURETICS	21	5	26	29.2
BETA – RECEPTOR BLOCKER	9	6	15	17.0
CALCIUM CHANNEL BLOCKER CCB	7	4	11	12.4
ACE – INHIBITOR	4	2	6	7%
BRINERDIN	3	2	5	5.6
CNS – ACTING	5	-	5	5.6
DIGOXIN	4	1	5	5.6
ACETYL SALICYLIC ACID (ASA)	3	1	4	4.5
ANXIOLYTIC	2	1	3	3.0
POTASSIUM CHLORIDE SLOW K/MIST. POT. CIT	3	-	3	3.0
MINIZIDE	1	1	2	2.2
MIST. MAG. TRISILICATE	2	-	2	2.2

Confidence Level (99%)

(-1.5, 16.4)

Mean _ - 7.42

6.12



E. 4 Desire for change in current Therapy and reason

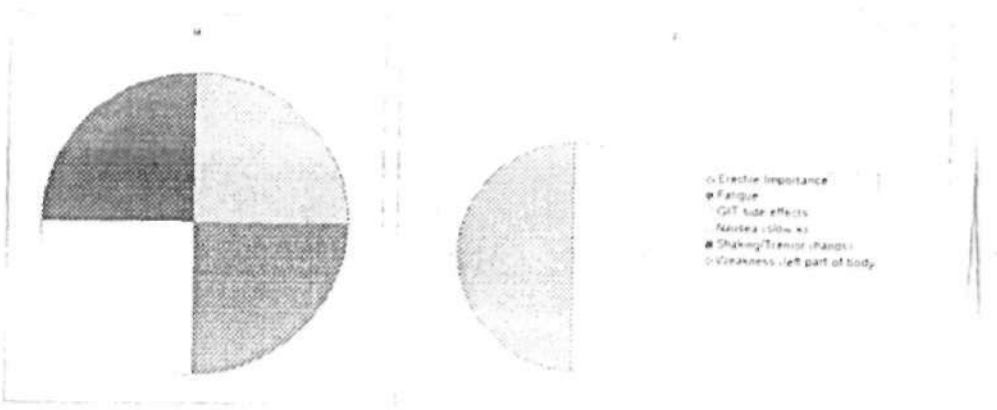
Side effects 6/41

No side effects 35/41

Type of side effect Freq.

Type of side of Effect

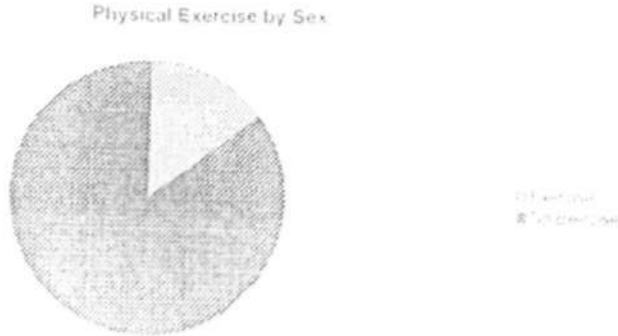
	F	M	Freq.
Erectile Importance	-	1	1
Fatigue	-	1	1
GIT side effects	-	1	1
Nausea (slow k)	1	-	1
Shaking/Tremor (hands)	-	1	1
Weakness (left part of body)	1	-	1
	2	4	6



F. **NON DRUG THERAPY**

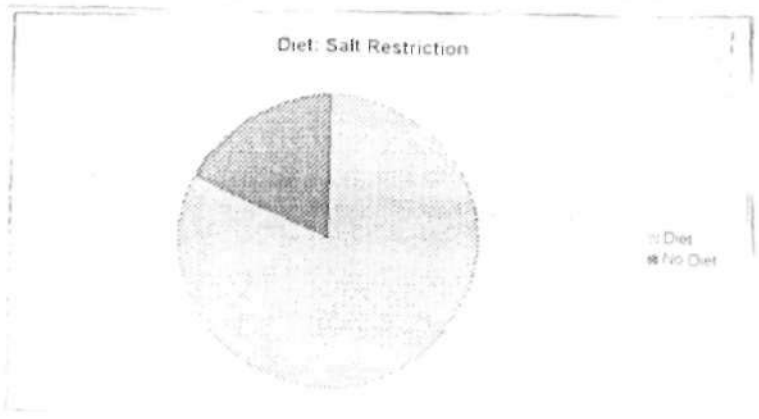
F 1 Physical Exercise: by Sex

	Freq.	%	Female	Male
Exercise	6	15	3	3
No Exercise	35	85	19	16
	41	**100**	22	19



F. 2 Diet: Salt restriction

		F	M	%
Diet	36	27	9	88
No Diet	5	3	2	12
	41	**50**	**11**	**100**



CHAPTER FOUR

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

4.1 DISCUSSION.

Factors that determine the protocol for the management of hypertension include personal data, family, social clinical and drug histories of the patient. This thesis surveyed in addition to there factors, the place of non-drug measures in the management of hypertension at the cardiac clinic of ABUTH, Zaria for the period of the survey.

The survey was conducted using a combination of retrospective evaluation of patient case histories and administration of questionnaire. Responses were obtained from a sample of known hypertensive patients who attended the clinic during the period of this study. 41 respondents were surveyed, of which were 31 females and 10 males. The responses were recorded, analysed and interpreted.

4.1.1 PERSONAL DATA ANALYSIS.

The predominance of females in the cardiac clinic could be because they seek medical attention more promptly than the male patients. Also, it could be that they are referred from the antenatal clinic with pregnancy associated problems. While the **"silent killer syndrome"** phenomenon of hypertension may be responsible for the low incidence in males, as hypertension can exist without showing any symptoms or signs.

This result correlates well with data that females show little rise in blood pressure till after menopause. And data from collaborative study between University of Ibadan and the government of western Nigeria, showed that from childhood to 45, there was greater percentage of hypertensive males than females about up to 60 years the trend was reversed and after 60 years and beyond, no clear pattern was found.

4.1.2 **The body mass index** (BMI) The result obtained could be due to high caloric intake and excessive fat intake . The Framingham study demonstrated that 20% excess over desirable

weight clearly imparted a health risk. And this increased the risk of premature death, hypertension, diabetes and certain types of cancer.

4.1.3 **Occupational Distribution :** The result obtained correlates well with studies which show an inverse relationship between socio-economic status, level of education, income and occupation with hypertension (Table A.4).

4.1.4 **Family History:** Our result on parental hypertension conform to those from studies which show that family history is a risk factor for development of hypertension. But a greater relationship has been shown to exist between siblings (brothers and sisters) than between parents and offspring.

The result obtained correlate well with established studies in which multiple pregnancies was found to be one of the causes of pregnancy - induced hypertension PIH. This is further strengthened by the finding that pregnancy - induced hypertension, PIH incidence is fairly high 43% (Table B.3) while pregnancy - aggravated hypertension was less (17%) . This is comparable to 3% incidence found in the literature, a level associated with a five - fold increase in the risk of developing pre - eclampsia (table B.4).

But even though their pregnancy caused the high blood pressure to manifest, those patients must have had other predisposing risk factors, for developing hypertension. But this was not investigated. But referral of such patients from the antenatal clinic were documented in their medical records. This was used to corroborate their responses in the interview and questionnaire survey.

4.1.5 **Social History analysis:**

Alcohol consumption: Alcohol intake was low (7%), cigarette - smoking was higher (17%). This could be because in the environment the religious beliefs of the patients discourages **alcohol consumption**. Also, female patients were found to predominate in the clinic and they are not known to be heavy drinkers, the incidence of alcoholic consumption was found to be really low.

Cigarette Smoking: This level of cigarette - smoking correlates with the findings by the study on smoking cassation in coronary artery disease. The data from these studies when analysed, showed that overall mortality was significantly more among ex - smokers than among non- smokers[244] . (Table C.2 and C.3)

Kolanut intake: The result obtained shows that 200mg caffeine elevates blood pressure by about 10/8mmgHg for 1 to 2 hours. But the combination of cigarettes and coffee produces greater and more lasting effect which is still present at 2.5 hours[245] (table C.4).

Salt intake: Findings by investigators[246] on the relationship of salt - intake with hypertension, though not compatible, strongly suggest that subjects with essential hypertension have a genetically determined defect in cell Membrane transport which leads to an increase intracellular sodium. The same defect can be detected in normotensive relatives of patients with hypertension. So, it has been suggested that this defect, in the presence of a high salt intake might eventually lead to changes in cell physiology which could cause hypertension (Table C.5).

Similar studies suggest that blood pressure is more closely related to the ratio of urinary sodium to potassium than to either electrolyte alone.

Inter-salt analysis showed that a reduction of the 24 - hour urinary sodium - potassium ratio 3:1, (170mmol of sodium 50mmol is associated with a 3.4 mmhg reduction in systolic blood pressure[247]. Also, hyperaemia could cause renal impairment in such patients.

4.1.6 **Clinical History Analysis:**

Age at diagnosis was 20 – 50 years for females and 30 – 60 years for malesOther studies show that blood pressure trends of an individual are determined very soon after birth. And that those whose pressure is at the upper end of the range as young adults may be destined to become the hypertensive of the future. This incidence could be related to family history, obesity diet and level of physical activity[248]. A study in a Nigeria town, Ilorin, Ibadan in 1960 also showed that blood pressure rose with age in both sexes[249]. Also, in most western populations, blood pressure is reported to rise with age, a positive relationship demonstrated by surveys and prospective studies, in most populations with diverse geographical, cultural and socioeconomic characteristics[250].

4.1.7 **Co existing Illness:** The incidence of **Co-existing illness** and **presenting complaints** of the patients correlate well with findings about organ damage associated with hypertension. The World Health Organisation, (WHO) reports that untreated hypertension increases the risk of vascular damage involving resistance and conduct anteriores. And the lesions lead to

cardiac, renal and cerebrovascular morbidity and mortality. The incidence of these different lesion is also dependent upon the level of other risk factors such as plasma cholesterol, diabetes and tobacco - smoking, in the community. In populations of industrialised countries, with high blood lipids most organ damage results from atherosclerotic and cardiac complications. But in other areas of the world like China, Russia and south America, cerebrovascular accidents are the frequent morbid signs of hypertension and malignant/accelerate hypertension is frequent. Whereas in developing countries, the incidence of cardiovascular disease is steadily increasing where programmes of detection, treatment and prevention of hypertension and other risk factors are not implemented.

4.1.8 Drug History Analysis

At Diagnosis: The result conforms with World Health Organisation WHO, guidelines The WHO[252 a, b] promotes the general agreement that five classes of drugs are most suitable for the first time treatment of patients with high blood pressure. They include diuretics, beta-blockers, ACE - inhibitors, calcium antogamists and alpha blockers. And that other classes of drugs may be used in certain situations.

Prescription change: According to the WHO[253], the treatment for hypertension is usually for life. Therefore, the patient and the physician are committed to a long association and it is important to establish effective communication with the patient. And to take into account the patients' psychological status and preferences in order to arrive at a mutually agreed regimen of treatment (good treatment goal and high patient compliance Tables E.1 and E.2). The 1999 WHO/ISH hypertension guidelines promote six main drug classes including diuretics, beta - blockers, ACE - inhibitor, calcium antogamists, alpha - blockers and angiotensin II antogamists) worldwide depending on cost and other factors. Also, the use of reserpine and methyldopa in other parts of the world are acknowledge by the guideline[254]. In addition, the hypertension optimal treatment (HOT) study suggest the use of low dose Aspirin (75mg once daily) in the hypertensive patient whose blood pressure has been rigorously controlled, who are at high risk of coronary heart disease (CHD), and who are not at risk of bleeding from the gastro-intestinal tract or from other sites[255]. (Table E.3).

4.1.9 **Non Drug Therapy Analysis**

Literature indicate that the overall strategy of management of hypertension involves initiation of lifestyle measures (Cessation of smoking, weight reduction moderation in alcohol consumption, reduction of salt intake and increased physical activity), in combination with drug treatment[257] . (Table F.1 and F.2).

4.2 CONCLUSION

From the processed data, the incidence of hypertension was found to conform to expectations; hypertension was age-related, females patients were preponderant, being of lower socio-economic class, less educated, had lower incomes compared to the male hypertensive patients who were few and had better occupations females were found to be more obese than the men. The men were mostly overweight, (BMI analysis).

'Physical exercise and weight-reducing diets' (restriction of fat and caloric intake) should be suggested to female patients. Incidence of familial hypertension was low suggesting that other factors were more important in the development of hypertension in this environment. But pregnancy associated hypertension was common. Thus, female hypertensive patients should be encourage to benefit from ante-natal care during pregnancy to reduce incidents of eclampsia and pre-eclampsia toxaemia, PET. In addition cases of post-partum congestive heart failure could be reduced through education on harmful traditional practices, such as consumption of potash in pap prepared for females after delivery of babies (i.e. post partum tradition).

'The social history of patients' revealed low intake of alcohol and low incidence of cigarette - smoking. This should be encouraged. But Kolanut, salt and potash intake were found to be high. Since these are risk factors for developing hypertension, patients should be strongly advised to restrict intake of these substances which contain caffeine, sodium chloride and potassium carbonate, respectively. Whereas caffeine is a pressor agent, the electrolytes cause homeostasis imbalance in renal hemodynamics.

'Patients clinical histories' revealed that first diagnosis of hypertension was common in females from 20 years of age. While it developed later in the male patients. This could be probably due to the low socio-economic status of the woman in this environment. And low socio-economic status has been reported to be inversely related to hypertension. Such women should be encouraged to improve their lot through education and economic empowerment.

'Evidence of target organ' damage was revealed by the incidence of co-existing illness and the presenting complaints of the patients congestive cardiac failure and visual disturbance were common. Therefore, patients should be encouraged by all health workers of the hospital to bring relatives to hospital for checks on their blood pressures in an attempt to create awareness about the high incidence of hypertension in the environment. Since early treatment prolongs life expectancy, minimises cost by reducing hospital admissions and prevent the need for rehabilitation following stroke, etc.

'The drug history of patients' revealed that the choice of drugs was in conformity with world standards within the constraints of affordability and availability which are recognised worldwide. For some of the recommended drugs; Also considering the environment and the status of the majority of the patients. The frequency with which prescriptions were changed indicates a reasonable level of patients - doctor interaction while prescriptions were mostly changed due to poor control (physician) and side - effects as well as poor compliance (patients).

'Incidence of side - effects' was low and could be further decreased by the use of combination of drugs from the WHO/ISH recommended list.

Non drug measures such as physical exercise should be more highly recommended than is presently the case as well as caloric and saturated fat restriction. But salt restriction was highly recommended and should be maintained. But dietary control especially saturated fat intake (fried foods, palm- oil Animal fat etc) should be reduced in the overweight and obese patients while risk factors such as Kolanut and potash consumption should be discouraged as it is not sound professional practice to allow consumption of pressor agents while treating a patient with antihypertensive drugs.

4.3 RECOMMENDATIONS

This thesis having found that hypertension is common in this environment recommends that the management of ABU Teaching Hospital should provide first - line drugs (Diuretics, methyldopa, beta-blocker) as well as new drugs such as (ACE - inhibitors and calcium antagonists in adequate amounts at affordable cost at all times in the hospital pharmacy.

This is because the WHO/ISH hypertension guidelines report evidence of beneficial effects on mortality and morbidity from randomised controlled trials with older antihypertensive (diuretics, methyldopa, beta - blockers). While evidence of benefit with newer drugs such as ACE - inhibitors and calcium antogamists is just beginning to accumulate.

Family history of hypertension especially among siblings could not be investigated because such information were not in the patient medical records. Therefore, the doctors should be encouraged to clerk patients in detail to facilitate determination of family history of hypertension such that appropriate preventive measures can be taken.

Also, general measures for the treatment of hypertension should be strongly recommended to patients attending the cardiac clinic.

Finally, ABU Teaching Hospital Management should be commended for their present protocol for management of hypertension but emphasis needs to be placed on lifestyle modification for obese and overweight patients. Such lifestyle measures are useful in four complimentary ways. They lower blood pressure in individual patients, reduce the need for antihypertensive drugs, they minimise associated risk factors in an individual and they constitute the primary prevention of hypertension and associated cardiovascular diseases in the population.

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APPENDIX I QUESTIONNAIRE

PLEASE READ THE QUESTIONS AND TICK THE ANSWER APPLICABLE TO YOU.

PERSONAL DATA

1. Age..... years. Weight..... Kg. Height.....m
2. Sex: Male ☐ Female ☐
3. Dietary Status: Nourished { } Malnourished { }
4. Occupation ----------

FAMILY HISTORY

5. Parents: Hypertensive Yes { } No { } (a) Mother { } Father { }
   Non - Hypertensive { }
6. Number of Children ----------

Answer the following if Female:

7. How many high pregnancies have you had ? ----------
8. Is your high blood pressure related to pregnancy ? Yes { } No { }
9. Does pregnancy make your hypertension worse ? Yes { } No { }

SOCIAL HISTORY

10. Do you take alcohol ? Yes { } No { }
11. Do you smoke (e.g cigarette. pipe. snuff ?) Yes { } No { }
12. Number of stick per day ----------
13. Do you chew kola ? (e.g Kolanut, bitter cola) Yes { } No { }
14. Do you like plenty of salt on your food ? Yes { } No { }
15. Do you add salt to your food at table ? Yes { } No { }
16. Do you use potash (Kanwa, kaun) in your cooking ? Yes { } No { }

CLINICAL HISTORY

17. Age at time of diagnosis ---------- years.
18. Do you have any other illness apart from HBP ? Yes { } No { }
19. If yes, what other illness do you suffer from ? Yes { } No { }

    1. ---------- 2 ---------- 3 ----------

    4. ---------- 5 ---------- 6 ----------

20. Presenting compliant (e.g stroke, CF, headache) ?

DRUG HISTORY

21. Drugs prescribed at time of Diagnosis

    1. ---------- 2 ---------- 3 ----------

    4. ---------- 5 ---------- 6 ----------

22. have your drugs ever been changed ? Yes { } No { }

23. How many times ? ----------

24. For what reason your drop changed ?

    Tick as applicable.

Poor compliance	{ }
No control of HBP	{ }
Side effects	{ }
Cost (too expensive)	{ }
Nature of your illness	{ }
Availability (scarce, out - of - stock)	{ }

25. What drugs are you taking now ? ---------- ----------

    ---------- ----------, ----------

26. Do you still want your drugs to be changed Yes { } No { }

27. If yes, why ? _____

NON - DRUG THERAPY

28. Is there any physical exercise you have been advised to do ?

    Yes { } No { }

29. Are you on any diet ? Yes { } No { }

30. What type of diet ? _____

APPENDIX 2 SPREADSHEET DATA

S/N	AGE	W	H	S	N	OCC	FH	NO.OF C.	NO.OF P.	PIH	PHA	SOCIAL HISTORY				
	years	kg	Metres	1. M	Y		1. Father					Alcohol	Smoking	# \day	K	Salt Corns
				2. F	N		2. Mother					Y	Y			
							3. Both					N	N			
							4. Neither									
1	47	67.7	1.51	2	Y	Tra	4	6\14	14	Y	N	N	Y	0.5	Y	N
2	63	73	1.62	1	Y	Tea	4	_	_	_	_	N	N	_	N	Y
3	56	68.8	1.59	1	Y	welder	4	_	_	_	_	N	N	_	Y	Y
4	46	88.9	1.55	2	Y	Tre	4	6	7	Y	N	N	N	_	N	Y
5	47	46	1.51	2	Y	H/W	4	_	_	_	_	N	Y	3.5	Y	Y
6	48	60.2	1.48	2	Y	H/W	4	4	10	Y	Y	N	N	_	Y	Y
7	62	75.8	1.54	2	Y	H/W	4	3	10	N	N	N	N	_	Y	Y
8	53	58.8	1.57	2	Y	Tra	4	9	12	Y	N	N	N	_	Y	Y
9	49	81	1.57	2	Y	Tra	4	7	7	N	N	N	N	_	Y	Y
10	50	59.8	1.75	1	Y	Landy	2	_	_	_	_	N	Y	5	N	N
11	70	60.4	1.61	1	Y	Tra	4	_	_	_	_	N	N	_	N	N
12	73	53.8	1.68	1	N	Farmer	4	_	_	_	_	N	N	_	Y	Y
13	49	60.4	1.52	2	Y	Tra	4	6	10	Y	N	N	N	_	N	N
14	57	42.2	1.46	2	Y	H/W	4	9	11	N	N	N	N	_	N	N
15	72	80.6	1.53	2	Y	Tra	4	6	11	N	N	N	N	_	Y	N
16	55	53.2	1.64	1	Y	Tailor	3	_	_	_	_	N	N	_	Y	N
17	42	69.6	1.61	2	Y	H/W	2	6	6	N	N	N	N	_	Y	N
18	55	47.7	1.52	2	N	H/W	4	1	1	N	N	N	N	_	Y	Y
19	48	50	1.52	2	Y	H/W	1Y\3F	10	10	N	N	N	N	_	Y	N
20	40	64.5	1.65	1	Y	Civil Servant	4	_	_	_	_	Y	Y	28	Y	N
21	21	34.2	1.5	2	Yw	H/W	4	2	2	N	N	N	N	_	Y	N
22	46	85.4	1.605	2	Y	H/W	4	5	6	Y	N	N	N	_	N	N
23	61	62.7	1.702	1	Y	Tra	4	_	_	_	_	N	N	_	Y	Y
24	50	65	1.6	2	Y	H/W	2	8	9	Y	N	N	N	_	Y	Y
25	75	51.8	1.51	2	Y	Tra	4	2	2	N	N	N	N	_	Y	N
26	62	90.4	1.65	1	Y	Plumber	2	_	_	_	_	Y	N	_	Y	Y

27	60	50	1.6	2	Y	HW	4	2	6	8	2	N	N	N	Y	–	N
28	59	65.4	1.59	2	Y	HW	4	8	12	6	N	N	N	N	Y	–	N
29	44	62.5	1.52	2	Y	Tra	4	6	6	4	Y	N	N	N	Y	–	N
30	62	45.7	1.6	2	Y	Tra	2	4	4	9	N	N	N	N	Y	–	Y
31	59	57.5	1.52	2	Y	Tra	3	9	10	5	Y	Y	N	N	N	–	Y
32	12	91.1		2	Y	HW	4	5	5	5	N	N	N	N	N	–	N
33	12	91.1	1.52	2	Y	HW	4	5	5	5	N	N	N	N	N	–	N
34	54			2	Y	Caterer	4	6	7	7	N	N	N	N	N	–	N
35	63	74.8	1.54	1	Y	Teach	4	8	–	–	–	N	N	N	Y	–	Y
36	55	71.9	1.52	2	Y	HW	4	9	12	6	N	N	N	N	Y	–	N
37	48	46.2	1.57	2	Y	Tra	2	3	6	6	N	N	N	N	Y	6	Y
38	80	83	1.51	2	Y	Tra	1 2 3	2	2	2	N	N	N	N	N	–	Y
39	70	7	1.54	2	Y	Tra	4	5	5	5	N	N	N	N	N	–	Y
40	49	54.7	1.6	2	Y	Tra	4	10	10	10	Y	N	N	N	Y	1	Y
41	37	73	1.54	2	Y	Tailor	1 3	4	8	8	Y	N	N	N	N	–	N
42	53	74.8	1.42	2	Y	HW	4	7	9	9	N	N	Y	N	N	–	Y
43	39	68.2	1.53	2	Y	HW	4	6	8	8	Y	N	N	N	N	–	Y

CLINICAL HISTORY																			
S plus	POT	AAD	AOI	TOI	Pc	RxAD	DRx	#	RFC	CRx	SRD	RFD	PE	Diet	TOD
N	Y	21	N	–	Cho. PHF	Bendro	Y	4	1 2	B	N	X	Y	Y	LS
Y	Y	41	N	–	Obe	Ald B	Y	3	1	M I	N		Y	Y	LS
Y	N	53	N	–	H/c D3V	HYD NIF B	Y	3	4	NM. I.ASA	Y		Y	Y	LS
Y	Y	29	N	–	H/E	BPR	Y		1 2	NM	N	–	N	Y	LS
Y	Y	45	Y	Stroke HHF	B. Vision	FR Iv. C.D R	Y	2	2	Cold sk	Y	wack LHS	Y	Y	RS
N	Y	32	N	–	taily B	B	N	–	–	Aldmo	N	–	N	Y	RS
Y	Y	60	N	CCF	Sob pale	Las Dg Capt	y	1	1	DBC Asa	N	–	N	Y	LS
Y	Y	45	Y	PUD	DOE post P	BSK	Y	1	3	Adult	N	–	N	Y	LS
Y	Y	35	Y	Rhem atism	H/e	BSK	N	–	–	mod Ind	N	–	N	Y	LS
N	N	33	N	–	H /e Dizz	H(IV) B C SK	Y	1	1	Poy B	N	–	N	Y	LS
N	N	56	Y	Malic Catarat	Trd.Pw.BV	VISK	Y	2		E I. Fatt inso	N	–	N	Y	LS
Y	Y	65	N	CCP 20 4T	Unc. H\E	NIF.PROPR	Y	3	3	Dis tr cap	Y		N	Y	LS
N	Y	42	N	AF EYE	Sub- ara hae	Ca Antag	Y	2	2 4	BPR	N	–	N	Y	LS
N	N	50	N	–	Cho SOB PP	B	Y	1	3 5	B	N	–	N	Y	LS
N	Y	65	N	–	H\E Dizz	Dig NIF SK	y	2	2	B	N	–	N	Y	LS
N	Y	44	Y	Img bills 4 male	F H	E pp	B. Loraz	Y	4	2	B	N	–	N	Y	LS
N	Y	28	N	–	H\E Dizz	Ald.B. Diaz	Y	3	1 3 5	Ald B	N	–	N	Y	LS
Y	Y	44	–	–	musc pain	MD B	Y	1	6	B	N	–	N	Y	LS
N	Y	40	N	–	he D.DOE C	MD. B	Y	2	2 3 5	C Ad mut	N	–	N	N	–
N	N	39	N	–	H/e	MD.B	Y	2	1 4	B MND	N	–	N	N	–
N	Y	14	Y	RHD	RHD	B.MD	N	–	–	DY SK	Y	Nausea (sk)	N	Y	S pot mg
Y	Y	40	Y	JT PAN	Dizz H/e	Dig .Fr	N	–	–	MOD ABA	N	–	N	N	–
Y	Y	32	Y N	ANXIETY	H/e	Diazp	Y	2	3 5	Ind Amut	N	–	N	Y	LS
Y	Y	44	Y	TB	Numbness	MD B	Y	6	2 3	MD B	N	–	N	–	–
N	Y	65	N	–	H\E bi V R	MD. B	Y	1	2	I B Yeast	N	–	N	N	–
Y	Y	50	N	–	Epistaxis	MD. B	Y	1	2	Nit. Cpt	N	–	Y	N	–

N	Y	50	N	–	Dizz	B, SK	N	–	–	B	N	–	N	Y	LS
N	Y	60	N	–	F D HIE DOE	Resetp, B	Y	2	2 3	MD. M., Prop	N	–	N	Y	LS
N	Y	28	N	–	PET	Pr, MIN	Y	3	2 4	PET	N	–	N	Y	LS
Y	Y	54	Y	CCF	HIE	B, Adalat	N	2	1	Dig p cap tr	N	–	N	Y	LS
Y	Y	42	N	–	HIE,I/Heat	B.Brom Ind	Y	3	1 2 3 4	BB IN	N	–	N	Y	LS
N	Y	37	N	–	Chest pain	N.F,B	Y	7	2 4	Mod adalat	N	–	N	Y	LS
N	Y	37	N	–	Glau., HIE	N.F, Acetaz	Y	7	2 4	Mod adalat	N	–	N	Y	LS
N	N	50	Y	Stroke	V, HIE, Palp	B.MD,SK	N	–	–	Asa mod	N	–	Y	N	
Y	Y	60	N	–	Bone pain	MD,B	Y	2	1 2	Mod adalat	N	–	N	Y	LS
N	Y	61	Y	Bll Glaw	–	MOD	N	–	–	Nif, adalat	N	–	N	Y	LS
Y	Y	48	N	–	O, Cou, pp	Dig Fru, sk	Y	2	3	B	N	–	N	Y	LS
–	Y	52	N	–	Oedema	Dig Fru, sk	Y	4	2 3	Mini bnner	N	–	Y	Y	LS
Y	Y	69	N	–	D,H,DOE, P	MD	Y	1	2	Bnner prop	N	–	Y	Y	LS
Y	Y	40	N	–	Pnd,H,DOE D	MD,B	Y	2	2 3	B	N	–	N	Y	RS
N	Y	17	N	–	HIE, Dizz	MD	Y	2	3 5	Dig B A m P	N	–	N	Y	LS
N	Y	37	N	–		MD B	Y	1	2	Adalat I B	N	–	N	Y	LS
N	Y	35	N	–			N	–	–	B pror	N	–	N	Y	LS

APPENDIX 2 SPREADSHEET DATA

S/N	AGE	W	H	S	N	OCC	FH	NO.OF C.	NO.OF P.	PIH	PHA	SOCIAL HISTORY				
	years	kg	Metres	1. M	Y		1. Father					Alcohol	Smoking	# \day	K	Salt Coms
				2. F	N		2. Mother					Y	Y			
							3. Both					N	N			
							4. Neither									
1	47	67.7	1.51	2	Y	Tra	4	6\14	14	Y	N	N	Y	0.5	Y	N
2	63	73	1.62	1	Y	Tea	4	_	_	_	_	N	N	_	N	Y
3	56	68.8	1.59	1	Y	welder	4	_	_	_	_	N	N	_	Y	Y
4	46	88.9	1.55	2	Y	Tre	4	6	7	Y	N	N	N	_	N	Y
5	47	46	1.51	2	Y	H/W	4	_	_	_	_	N	Y	3.5	Y	Y
6	48	60.2	1.48	2	Y	H/W	4	4	10	Y	Y	N	N	_	Y	Y
7	62	75.8	1.54	2	Y	H/W	4	3	10	N	N	N	N	_	Y	Y
8	53	58.8	1.57	2	Y	Tra	4	9	12	Y	N	N	N	_	Y	Y
9	49	81	1.57	2	Y	Tra	4	7	7	N	N	N	N	_	Y	Y
10	50	59.8	1.75	1	Y	Landy	2	_	_	_	_	N	Y	5	N	N
11	70	60.4	1.61	1	Y	Tra	4	_	_	_	_	N	N	_	N	N
12	73	53.8	1.68	1	N	Farmer	4	_	_	_	_	N	N	_	Y	Y
13	49	60.4	1.52	2	Y	Tra	4	6	10	Y	N	N	N	_	N	N
14	57	42.2	1.46	2	Y	H/W	4	9	11	N	N	N	N	_	N	N
15	72	80.6	1.53	2	Y	Tra	4	6	11	N	N	N	N	_	Y	N
16	55	53.2	1.64	1	Y	Tailor	3	_	_	_	_	N	N	_	Y	N
17	42	89.6	1.61	2	Y	H/W	2	6	6	N	N	N	N	_	Y	N
18	55	47.7	1.52	2	N	H/W	4	1	1	N	N	N	N	_	Y	Y
19	48	50	1.52	2	Y	H/W	1Y\3F	10	10	N	N	N	N	_	Y	N
20	40	64.5	1.65	1	Y	Civil Servant	4	_	_	_	_	Y	Y	28	Y	N
21	21	34.2	1.5	2	Yw	H/W	4	2	2	N	N	N	N	_	Y	N
22	46	85.4	1.605	2	Y	H/W	4	5	6	Y	N	N	N	_	N	N
23	61	62.7	1.702	1	Y	Tra	4	_	_	_	_	N	N	_	Y	Y
24	50	65	1.6	2	Y	H/W	2	8	9	Y	N	N	N	_	Y	Y
25	75	51.8	1.51	2	Y	Tra	4	2	2	N	N	N	N	_	Y	N
26	62	90.4	1.65	1	Y	Plumber	2	_	_	_	_	Y	N	_	Y	Y

27	60	50	1.6	2	Y	H/W	4	2	2	N	N	N	N	_	Y	N
28	59	65.4	1.59	2	Y	H/W	4	8	12	N	N	N	N	_	Y	N
29	44	62.5	1.52	2	Y	Tra	4	6	6	Y	Y	N	N	_	Y	N
30	62	45.7	1.6	2	Y	Tra	2	4	4	N	N	N	N	_	Y	N
31	59	57.5	1.52	2	Y	Tra	3	9	10	Y	Y	N	N	_	Y	Y
32	12	91.1	.	2	Y	H/W	4	5	5	N	N	N	N	_	Y	Y
33	12	91.1	1.52	2	Y	H/W	4	5	5	N	N	N	N	_	N	N
34	54			2	Y	Caterer	4	6	7	N	N	N	N	_	N	N
35	63	74.8	1.54	1	Y	Teach	4	8	_	_	_	N	N	_	N	N
36	55	71.9	1.52	2	Y	H/W	4	9	12	N	N	N	N	_	Y	Y
37	48	46.2	1.57	2	Y	Tra	2	3	6	N	N	N	N	_	Y	N
38	80	83	1.51	2	Y	Tra	1 2 3	2	2	N	N	N	Y	6	Y	Y
39	70	7	1.54	2	Y	Tra	4	5	5	N	N	N	N	_	Y	Y
40	49	54.7	1.6	2	Y	Tra	4	10	10	Y	N	N	N	_	Y	Y
41	37	73	1.54	2	Y	Tailor	1 3	4	8	Y	Y	N	Y	1	Y	Y
42	53	74.8	1.42	2	Y	H/W	4	7	9	N	N	Y	N	_	N	Y
43	39	68.2	1.53	2	Y	H/W	4	6	8	Y	N	N	N	_	Y	N

Sz.Rel. ABRAHAM Lin

CLINICAL HISTORY																		
S plus	POT	AAD	AOI	TOI	Pc	RxAD	DRx	#	RFC	CRx	SRD	RFD	PE	Diet	TOD			
N	Y	21	N	–	Cho. PHF	Bendro	Y	4	1 2	B	N		X	Y	LS			
Y	Y	41	N	–	Obe	Ald B	Y	3	1	M I	N		Y	Y	LS			
Y	N	53	N	–	H/c D3V	HYD NIF B	Y	3	4	NM, 1.ASA	Y		Y	Y	LS			
Y	Y	29	N	–	H/E	BPR	Y		1 2	NM	N	–	N	Y	LS			
Y	Y	45	Y	Stroke HHF	B. Vision	FR Iv. C,D R	Y	2	2	Cold sk	Y	wack LHS	Y	Y	RS			
N	Y	32	N	–	fatty B	B	N	–	–	Aldmo	N	–	N	Y	RS			
Y	Y	60	N	CCF	Sob pale	Las Dg Capt	Y	1	1	DBC Asa	N	–	N	Y	LS			
Y	Y	45	Y	PUD	DOE post P	BSK	Y	1	3	Adult	N	–	N	Y	LS			
Y	Y	35	Y	Rhem atism	H/e	BSK	N	–	–	mod Ind	N	–	N	Y	LS			
N	Y	65	N	–	HE bl V R	MD. B	Y	1	2	1 B Yeast	N	–	N	N	–			
Y	Y	50	N	–	Epistaxis	MD. B	Y	1	2	Nit. Cpl	N	–	Y	N	–			
Y	Y	45	Y	PUD	DOE post P	BSK	Y	1	3	Adult	N	–	N	Y	LS			
N	N	33	N	–	H /e DIzz	H(IV) B C SK	Y	1	–	Pay B	N	–	N	Y	LS			
N	N	56	Y	Malic Cabaret	Trd.PW.BV	VISK	Y	2		E.I. Fatt inso	N	–	N	Y	LS			
Y	Y	65	N	CCP 20 4T	Unc. HE	NIF.PROPR	Y	3	3	Dis ft oap	Y		N	Y	LS			
N	Y	42	N	AF EYE	Sub- ara hae	Ca Antag	Y	2	2 4	BPR	N	–	N	Y	LS			
N	N	50	N	–	Cho SOB PP	B	Y	1	3 5	B	N	–	N	Y	LS			
N	Y	65	N	–	HE Dizz	Dig NIF SK	Y	2	2	B	N	–	N	Y	LS			
N	Y	44	Y	Ing bills 4 male	F HE pp	B. Lovaz	Y	4	2	B	N	–	N	Y	LS			
N	Y	28	N	–	HE Dizz	Ald.B. Diaz	Y	3	1 3 5	Ald B	N	–	N	Y	LS			
Y	Y	44	–	–	musc pain	MD B	Y	1	6	B	N	–	N	Y	LS			
N	Y	40	N	–	hig D.DOE C	MD. B	Y	2	2 3 5	C Ad mut	N	–	N	N	–			
N	N	39	N	–	H/e	MD.B	Y	2	1 4	B MND	N	–	N	N	–			
N	Y	14	Y	RHD	RHD	B.MD	N	–	–	DY SK	Y	Nausea (sk)	N	Y	S pot mg			
Y	Y	40	Y	JT PAN	Dizz H/e	Dig .Ft	N	–	–	MOD ABA	N	–	N	N	–			
Y	Y	32	Y N	ANXIETY	H/e	Diazp	Y	2	3 5	Ind Anut	N	–	N	Y	LS			
Y	Y	44	Y	TB	Numbness	MD B	Y	6	2 3	MD B	N	–	N	–	–			
N	Y	65	N	–	HE bl V R	MD. B	Y	1	2	1 B Yeast	N	–	N	N	–			
Y	Y	50	N	–	Epistaxis	MD. B	Y	1	2	Nit. Cpl	N	–	Y	N	–			