IDENTIFICATION OF FACTORS AFFECTING BLOOD PRESSURE CONTROL IN PATIENTS ADMITTED WITH HYPERTENSION IN PENANG GENERAL HOSPITAL

by

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DEDICATION

This work is dedicated to my father, my brother Salah and Yasir, my sisters Zobaida, Kaother, Emtithal, Amani and Etidal. To my lovely nieces and nephews Mohris, Mohd. Yahya, Montasir, Mohd. Motasim, Ahmad, Hassanat, Amna, Iya and Tasneem.

Thanks for love, inspiration and doa

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LIST OF ABBREVIATIONS

ACEIs	**Angiotensin converting enzyme inhibitors**
ARBs	**Angiotensin II receptor blockers**
BBs	**Beta blockers**
BP	**Blood pressure**
CCBs	**Calcium channel blockers**
DBP	**Diastolic blood pressure**
IHD	**Ischemic heart disease**
HDL	**High density lipoprotein**
LDL	**Low density lipoprotein**
MAP	**Mean arterial blood pressure**
mmHg	**Millimeter mercury**
mmol	**Millimole**
SBP	**Systolic blood pressure**
TIA	**Transient ischemic attack**

Pengenalpastian faktor-faktor yang mempengaruhi kawalan tekanan darah dikalangan pesakit darah tinggi di Hospital Besar Pulau Pinang

Abstrak

Matlamat rawatan hipertensi ialah untuk memulih kembali tekanan darah dan mencegah komplikasi kardiovaskular dan renal. Secara praktik, matlamat ini sukar dicapai seperti yang digambarkan oleh kajian-kajian di klinik masyarakat dan pesakit luar. Pengenalpastian faktor-faktor berhubung dengan kawalan hipertensi adalah penting dalam rawatannya. Banyak kajian yang diterbitkan sehingga kini berfokuskan pesakit luar dengan hanya sebilangan kecil bertumpu pada pesakit yang masih dirawat. Tujuan kajian ini ialah untuk menyiasat keberkesanan kawalan hipertensi dikalangan pesakit yang dimasukkan ke Hospital Besar Pulau Pinang serta menentukan faktor-faktor yang mempengaruhi kawalan hipertensi dikalangan pesakit berkenaan. Empat ratus orang pesakit hipertensi kronik yang dimasukkan ke wad perubatan dipilih berturut-turut menyertai kajian ini. Mereka di pantau sehingga hari mereka dibenarkan pulang. Bacaan tekanan darah diperolehi dari rekod kesihatan sewaktu kemasukkan dan secara harian sehingga pesakit dibenarkan pulang. Maklumat lain yang diambil termasuklah data demografik, keadaan morbiditi, kerosakan organ sasaran, faktor risiko kardiovaskular, dan rawatan antihipertensi. Statistik deskriptif digunakan bagi menentukan ciri-ciri pesakit. Ujian student-T and Chi square digunakan untuk membandingkan angkubah berterusan dan frekuensi peratusan angkubah nominal masing-masing.

Regressi logistik digunapakai untuk menentukan peramal kawalan hipertensi. Keputusan menunjukkan bahawa 48.5% pesakit adalah lelaki manakala umur min ialah 59 ± 11 tahun. 39.6% pesakit adalah berbangsa Melayu, 36% berbangsa Cina dan 24.5% berbangsa India. Majoriti pesakit sudah berkahwin (82.3%). Lebih daripada separuh pesakit (51.5%) menerima pendidikan sekolah rendah. 44.5% pesakit terdiri dari surirumah. Hipertensi baru didagnosa dalam 5.5% pesakit manakala 4.8% pesakit menderita hipertensi kurang dari setahun. 60% pesakit menderita hipertensi antara 1 hingga 10 tahun dan 23.8% mengalami hipertensi lebih dari 10 tahun sementara untuk 6% pesakit pula, jangkawaktu hipertensi tidak diketahui. Lebih kurang 10% pesakit dimasukkan ke wad kurang dari 5 hari. Tekanan darah dapat dikawal dikalangan 24% pesakit semasa kemasukan dan 54% pesakit semasa pesakit dibenarkan pulang. Analisa multivariate pada kemasukkan menunjukkan bahawa peramal kawalan tekanan darah adalah penggunaan diuretik dan statin. Faktor yang dikenalpasti berkaitan dengan kurang kawalan tekanan darah adalah bangsa Melayu, diabetes, penyakit serebrovaskular, retinopati dan bilangan ko-morbiditi. Analisa Multivariate pada masa pulang menunjukkan bahawa peramal kawalan tekanan darah yang baik adalah diuretik dan perencat beta manakala peramal kurang kawalan tekanan darah ialah diabetes, penyakit ginjal kronik, nefropati diabetik, penyakit serebrovaskular dan bilangan ko-morbiditi. Keputusan-keputusan ini menunjukkan bahawa hipertensi yang tidak terkawal dikalangan pesakit hospital dan kawalan tekanan darah adalah lebih baik semasa pesakit dibenarkan pulang daripada semasa kemasukan. Wanita, berbangsa Melayu, pesakit dengan diabetes, penyakit renal dan strok lebih berkemungkinan mengalami kurang kawalan hipertensi .

Identification of factors affecting blood pressure control in patients admitted with hypertension in Penang General Hospital

Abstract

The goal of treatment of hypertension is to normalize the blood pressure and to prevent cardiovascular and renal complication. This goal is difficult to achieve in practice as shown by studies in the community and outpatients clinics. Identification of factors related to hypertension control is important in treatment of hypertension. Many studies published so far were done in outpatients with few studies on inpatients. The aim of this study was to investigate the adequacy of hypertension control in patients admitted to Penang General Hospital and to determine factors affecting hypertension control among these patients.

Four hundred consecutive hypertensive patients admitted in medical wards in Penang General Hospital were included in the study. They were followed until the day of discharge. Blood pressure readings were extracted from medical records on admission and daily until the day of discharge. Other informations taken were demographic data, comorbid conditions, target organ damage, cardiovascular risk factors and antihypertensive treatment. Descriptive statistic was used to determine patients characteristic. Parametric and non parametric tests were used when applicable. Logistic regression was used to determine predictors of hypertension control. The results showed that 48.5% of the patients were male, the mean age was 59± 11 years, 39.6% were Malay, 36% were Chinese and 24.5% were Indian. The majority of patients were married (82.3%). More than half of the patients (51.5%) received primary school education only. House wives represent 44.5% of the sample. Hypertension was

newly diagnosed in 5.5%, 4.75% had hypertension for less than 1 year, about 60% had hypertension for 1 to 10 years and 6% unknown 23.75% had hypertension for more than 10 years. More than half of the patients (54%) were admitted for less than 5 days. Blood pressure was controlled in 24% on admission and in 54% of patients on discharge. Multivariate analysis on admission revealed that the predictors of BP control were the use of diuretics and statin. Factors identified to be associated with poor blood pressure control were Malay, diabetes, cerebrovascular disease, retinopathy and number of comorbidities. Multivariate analysis on discharge showed that the predictors of good BP control were diuretics and beta- blockers and the predictors of poor BP control were diabetes, chronic kidney disease, diabetic nephropathy, cerebrovascular disease and number of comorbidity. These results demonstrated that hypertension was poorly controlled among inpatients and that BP control was better on discharge than on admission. Malay, patients with diabetes, renal disease and cerebrovascular disease were more likely to have poor hypertension control.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Hypertension is defined as a persistent systolic blood pressure reading (SBP) of 140 mmHg or greater and or a diastolic blood pressure reading (DBP) of 90 mmHg or greater and or taking of antihypertensive medication, (JNCVII, 2003). Hypertension is divided into two main categories i.e., essential hypertension and secondary hypertension. Essential hypertension occurs in 90% of the cases and has no identifiable causes, while secondary hypertension occurs in the remaining 10% of the cases and has identified causes.

1.2 Classification of hypertension

The seventh Report of The Joint National Committee on Prevention, Detection, Evaluation and Treatment of high blood pressure classified blood pressure into four categories namely , normal, prehypertension, stage one hypertension and stage two hypertension. The normal category refers to blood pressure ranges of less than 120/80 mmHg, prehypertension is in the 120-139/80-89 mmHg range, stage one is 140-159/ 90-99 mmHg range and stage two is blood pressure equal to or more than 160/100 mmHg (JNCVII, 2003). This classification is based on average of two or more measurement on two or more office visits. Patients with prehypertension are at increased risk of progression to hypertension (JNCVII, 2003). They are twice more likely the risk to develop hypertension as those at a lower value (Vasan et al, 2001).

1.3 Prevalence of hypertension

Hypertension affects about 1 billion individuals worldwide. In the United States the National Health and Nutrition Examination Survey (NHANES1988-2000) reported that hypertension prevalence was 31.3% with an estimates of 65 million American having hypertension (Fields et al. 2004). Of hypertensive subjects 68.9% were found to be aware of their condition, 58.4% were on treatment and 31% had controlled their hypertension (Hajjar and Kotchen, 2003).

In Malaysia, The National Health and Morbidity survey of 21,391 individuals over the age of 30 in 1996 showed a high prevalence of high blood pressure with 33% of adults having hypertension. Among hypertensive individuals, 33% were aware of their hypertension, 23% were on treatment while only 6% had controlled their hypertension (Lim et al, 2004). In China, the prevalence of hypertension was found to be 27.2% in the adult population aged between 35 to 74 years of these 44.7% were aware of their condition, 28.2% were on treatment while only 8.1% had their blood pressure under control (Gu et al, 2002). In a survey of rural Filipinos (age 30 and more), the prevalence of hypertension was found to be 23%, 42% were diagnosed, 47% were on treatment, while blood pressure was controlled in 35% of the treated patients and in 17% of all hypertensive patients (Reyes-Gibby and Aday 2000). Awareness of hypertension is important to control blood pressure. Many patients are not aware of their condition leading to a low rate of hypertension control. In some communities about half of the patients were not aware of their condition. For instance, among the Parsi community of India, the prevalence of

hypertension was 36.4% of which 48.5% were not aware of their condition. Among those who were aware, 36.4% were not compliant and only 13.6% had controlled their hypertension (Bharucha and Kuruvilla 2003).

Hypertension is a leading cause of morbidity and mortality with microvascular and macrovascular complication which includes coronary artery diseases, nephropathy, retinopathy, and neuropathy. Hypertension is rarely present without other accompanying risk factors. There is a strong association between hypertension and diabetes mellitus, as many studies have reported a high prevalence of diabetes mellitus among hypertensive patients (Ghannem and Hadj, 1997, Gavalda et al, 1993, Mafauzy et al, 2003). Furthermore, a study conducted in a primary care clinic in Malaysia reported that 67% of patients with type 2 diabetic patients had hypertension (Chan, 2005).

A survey on the epidemiology of hypertension in Tunisia reported that 10.2% of the subjects were diabetic, 27.7% were obese, 56.7% were overweight and 21.5% were smokers (Ghannem and Hadj, 1997). Another study on hypertensive patients in their first visit to a hypertension unit in Spain, showed that family history was present in 53%, a sedentary life style in 52%, high cholesterol levels in 37%, smoking in 35%, obesity in 33%, left ventricular hypertrophy in 16%, alcohol consumption in 13% and diabetes mellitus in 11% (Gavalda et al, 1993). In a study in Kelantan, hypertension was found to be associated with the high prevalence of diabetes mellitus (19%), obesity (39.4%) and hypercholesterolemia (70.7%) (Mafauzy et al, 2003).The presence of other risk factors affects the incidence of hypertension. In a longitudinal study in

Japan, 4857 normotensive subjects were followed up for two years from 1997 to 1999 to determine the effect of the clustering of risk factors on blood pressure. It was found that a family history of hypertension, obesity, diabetes mellitus, hypercholesterolemia and hypertriglyceridemia were associated with the elevation of blood pressure and that the number of risk factors was positively associated with the increase in the level of both systolic and diastolic blood pressure (Tozawa et al, 2002). In a study in an urban health clinic in the Pacific Northwest, hypertensive patients were found to have diabetes mellitus, depression, heart disease and renal disease more than did non hypertensive patients (Rhoades et al, 2003).

1.4 Blood pressure control

According to JNC VII Report (2003) and The Malaysian Clinical Practice Guidelines on the management of hypertension (2002) the goal of blood pressure is 140/90 mmHg for patients without diabetes mellitus and without kidney disease, 130/80 mmHg for patients with diabetes mellitus and 125/75 mmHg for those with proteinuria of more than 1g/24 hours. Most patients need two or more antihypertensive drugs to achieve these goals (JNC VII, 2003). Blood pressure is considered controlled only when these goals are achieved.

The goal of therapy is to normalize blood pressure and to prevent cardiovascular events. In clinical trials, antihypertensive therapy was associated with a 35% to 40% mean reduction in stroke incidence, a 20% to 25% reduction in myocardial infarction, and a more than 50% reduction in heart failure (Phillips et al 2001). However in clinical practice, blood pressure control is difficult to

achieve. National and international surveys continue to reveal that hypertension is under diagnosed, patients diagnosed are often not treated and those treated are often not satisfactorily controlled (Murlow, 1998). For example globally less than 30% of treated hypertensive achieves BP targets (Burt, et al, 1995). A study on hypertension in 9 primary health care centers in Bahrain found that of 281 treated patients, only 16.5% had controlled blood pressure (Khaja et al, 2003).

Many studies have been conducted to identify the causes of uncontrolled blood pressure. It showed that many factors contribute to uncontrolled blood pressure. Most of these factors relate to the patients while others relate to health care providers. A Japanese survey on the impact of antihypertensive side effects found that 49% of patients with well controlled BP had at least one side effect with a current antihypertensive agent, whereas a significantly greater percentage of patients (61%) whose BP was poorly controlled tend to have a higher incidence of side effects (Toyoshima et al, 1997). The main cause of uncontrolled hypertension in many studies was the patient's non compliance (Joshi et al 1996).

Non compliance and medication side effects were among patient's factors that affect blood pressure control. These factors include factors that can be modified and that cannot be modified. Non modifiable factors include age, gender, ethnicity and family history. Modifiable factors include compliance, access to health care, and life style. Blood pressure control is also affected by physician factors. All these factors will be discussed in the following section.

1.5 Patient's factors

1.5.1 Age

The prevalence of hypertension increases with age as will the risk of cardiovascular disease. For individuals aged 40 to 70 years, each increment of 20 mmHg in systolic BP or 10 mmHg in diastolic BP doubles the risk of cardiovascular disease across the entire BP range from 115/75 to 185/115 mmHg. An individual who is normotensive at 55 years of age has a 90% risk for developing hypertension in his/her remaining lifetime (JNC VII Report, 2003). In cross-sectional and longitudinal population studies, systolic blood pressure increases until the age of 80 years while diastolic blood pressure increases only until 50 years old, then it either becomes constant or decreases slightly (Stasessen, et al, 2003). This is consistent with the data from a Malaysian survey in 1996 in which systolic blood pressure was found to increase with increasing age with diastolic blood pressure tending to decline beyond the age of 50-55 years (Lim, et al 2004). In the Framingham Heart Study, it was observed that the main predictor of cardiovascular risk changes from diastolic pressure to systolic pressure and then to pulse pressure with increasing age (Hyman and Pavlic, 2001). Below the age of 50, diastolic pressure was the strongest predictor. In contrast, between the 50-59 age group all three blood pressure indices were similar predictors, while from 60 years onwards, diastolic pressure was negatively related to the risk of coronary events, so that pulse pressure become a superior predictor compared to systolic pressure (The World Heath Report, 2002).

Hypertension occurs in more than two thirds of individual above 65 years (Hayman and Pavlic, 2001). However several randomized controlled trials showed that the treatment of hypertension in the elderly aged up to 84 years reduces stroke and cardiovascular morbidity and mortality (Kostis, et al 1997). Elderly patients are more susceptible to side effects than younger ones and the most common problem in the elderly is postural hypotension. As such, drug which may cause postural hypotension should be used with caution in this age group (National High Blood Pressure Education Program Working Group Report on Hypertension in elderly, 1994). The goal of treatment in older patients should be the same as in younger patients. In older patients an initial SBP below 160 mmHg is acceptable and attempts should be made to reduce BP to target levels of less than /or equal to 140/90 mmHg (Whelton et al 1998). Lifestyle measures should be offered to all older patients and they are as effective in the elderly as in younger patients (Whelton et al 1998). Thiazide diuretics and dihydropyridine CCBs are especially effective at lowering BP in older patients (Staessen et al, 1997). However, other drugs also have been shown to be effective (Wing, et al, 2003). From 65 years onwards it becomes more difficult to control blood pressure with treatment (Staessen, et al 1997) and many studies show that blood pressure control decreased with age (Lane et al, 2001 and Lloyd -Jones et al, 2005). In a study of hypertensive patients in Framingham Heart Study in 1990, hypertension control rates among those younger than 60 years, those aged between 60 and 79 years and those aged 80 years and older were 38%, 36% and 38% respectively in men and 38%, 28% and 23% respectively in women (Lloyd-Jones et al, 2005). Even in compliant patients, blood pressure control was found to be difficult in old people and such control decreased with

aging. In a study of hypertensive compliant men who attended the Veterans Affair Centre, hypertension was controlled only in 34.8% of patients. the rate of hypertension control in patients of less than 60 years was 42.1%, while for those between 60 and 75 years, it was 33.7% and for those older than 75 years, it was 29.4% (Bizien et al, 2004). Good hypertension control in primary care was associated with those aged 60 years and younger (Ornstein et al, 2004). Systolic blood pressure is better controlled in younger than in older individuals, while diastolic blood pressure is better controlled in older patients (Ayodele et al, 2005, and Alexander et al 1999). In a retrospective study of 1700 hypertensive patients in California, systolic blood pressure was controlled in 40% of those younger than 65 years and only in 26% of those aged 65 years and older, while diastolic blood pressure was controlled in 63% of the younger group and in 83% of the older group (Alexander et al, 1999).

1.5.2 Gender

The prevalence of hypertension is more common in men compared to women until the age of 55 years. With aging, it begins to shift. That is because female sex hormones offer cardiovascular protection. The loss of estrogen at menopause causes a more rapid increase over the time in systolic pressure in women than in men. In fact, pre menopausal women have lower systolic blood pressure than men, while diastolic blood pressure does not differ in either pre or post menopausal women. Before the age of 45, men have higher systolic blood pressure than women while after age of 45 years old, women have a higher systolic blood pressure (Ibrahim et al, 1995). In Malaysia, overall control of hypertension is low in women compared to men (Lim et al, 2004). Men tend to

have better control of systolic blood pressure, and combined blood pressure control and poorer control of diastolic blood pressure than women (Alexandar et al, 1999). However, other studies found that the male gender is associated with poor blood pressure control (Ibrahim et al, 1995).

1.5.3 Ethnicity

Most surveys showed that people of African origin have higher levels of blood pressure and a higher prevalence of hypertension than do those of white population (Primatista et al, 2000 and Cappuccio et al, 1997). They also have a higher rate of complications such as renal failure (Shulman et al, 1991) and left ventricular hypertrophy, (Kizer et al, 2004). A Black hypertensive is particularly sensitive to dietary salt restriction (Luft et al, 1991). They respond better to thiazide/ thiazide like diuretics or calcium channel blockers than to beta-blockers (Materson et al, 1993) or ACE inhibitors (Brown, 2000 and Hansson et al, 2000). This is consistent with the finding from a study in Yale in which it was found that older black subjects respond better to diuretics and calcium channel blockers than to beta- blockers and ACE inhibitors, while white subjects especially younger individuals respond better to ACE inhibitors and beta-blockers. This difference in response disappears when a small amount of diuretics is added to other antihypertensive medication (Moser, 1995).

Studies also show that British Asians have a higher mean blood pressure and hypertension prevalence than the white population (Primatesta et al, 2000, Cappuccio et al, 1997). They also have an increased risk of stroke and coronary heart disease (CHD) than the whites do (Cappuccio et al, 2002). In a study of hypertension in young adults in Singapore, Malays were found to have higher

prevalence of hypertension than Chinese and Indians (Gan et al, 2003) the same findings were also reported in Malaysia (Lim et al, 2004). In general blood pressure control in Malays was found to be lower (4%) compared to that in Chinese (7%) and Indians (9%) (Lim et al, 2004).

1.5.4 Diabetes Mellitus

Hypertension commonly occurs in diabetic patients. It affects about 20-60% of patients with diabetes mellitus depending on obesity, ethnicity, and age. Hypertension in type 2 diabetes mellitus occurs as a part of metabolic syndrome. While, hypertension in type 1 diabetes mellitus usually reflects the presence of diabetic nephropathy (American Diabetes Association, 2004). In a study of hypertension in type 1 diabetes population compared to general population in US, individuals with type 1 diabetes mellitus had more hypertension (43% vs. 15%), albuminuria (13.6% vs. 2.2%) and macroalbuminuria (8.1% vs. 0.4%) than did non diabetic individuals (Maahs et al, 2005). The presence of hypertension increases the risk of morbidity and mortality. In type 1 diabetes mellitus, the incidence of hypertension increases with the increase in the duration of diabetes mellitus from 5% at 10 years to 33% at 20 years and 70% at 40 years (Hypertension in Diabetic Study, 1993).

Hypertension is more prevalent in type 2 diabetes mellitus. The Hypertension in Diabetic Study group report a 39% prevalence of hypertension among newly diagnosed patients, and, in approximately half of them, the elevated BP reflects the onset of microalbuminuria and was strongly associated with obesity (Hypertension in Diabetic Study, 1993 and National High Blood Pressure Program Working Group report on Hypertension in Diabetes Mellitus, 1994).

Numerous studies have cited the need for hypertension to be detected and treated early in diabetes mellitus to prevent cardiovascular disease and to delay the onset of diabetic nephropathy. In fact, it is recommended that the treatment of hypertension in diabetes mellitus should be started if blood pressure is equal to or more than 130/80 mmHg (JNCVII, 2003, Standard of Medical care for Patients with diabetes mellitus, 2002 and Malaysian Clinical Practice Guidelines on The Management of Hypertension 2002). The presence of microalbuminuria or overt proteinuria should be treated even if blood pressure is not elevated, (Malaysian Clinical Practice Guidelines on The Management of Hypertension, 2002). In diabetic hypertensive patients, a lower target blood pressure is needed to get maximum reduction in development of cardiovascular and diabetic renal disease. The target of less than 130/80 mmHg is difficult to achieve but multiple drug prescription may assist in the attainment of this target (Bakris et al, 2000).

The choice of drugs should be individualized according to patient's comorbidities. Diuretics, beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) can be used to achieve the target blood pressure. ACEIs are the drugs of choice due to their cardiovascular and renal protective effects in diabetic patients while in those who do not tolerate ACEIs, ARBs can be used (JNC VII, 2003, Malaysian Clinical Practice Guidelines on the Management of Hypertension, 2002).

Diuretics can be used alone or in combination therapy. They should preferably be used with the lowest possible dose to minimize their metabolic side effects

which can be reduced when diuretics are used in combination with ACEIs or ARBs (Lind et al, 1994). Beta-blockers may be used initially when ACE or ARB cannot be used but they should be used with caution because of their side effects especially in type 1 diabetes mellitus (Lind et al, 1994). Calcium channel blockers (CCBs) have no metabolic side effect and they may be useful in patients with coronary heart disease (Hansson et al, 1998). Non dihydropyridine CCBs may be superior to dihydropyridine CCBs in reducing proteinuria in diabetic nephropathy (Bakris et al, 1998).

Numerous studies show that hypertension is difficult to be controlled in diabetic patients. For instance, a study in general medicine clinics found that diabetic patients were more likely to have uncontrolled hypertension than did non diabetic patients (Hicks et al, 2004). In another study only 25% of diabetics had their blood pressure controlled compared to 31% of all hypertensive patients (Hajjar and Kotchen 2003). Another study on a cohort of 1090 diabetic patients in primary care clinics reported that hypertension was controlled in 40% of the patients surveyed (Duggirala et al, 2005). In a study in a hospital hypertension unit in Spain, only 10.5% of diabetic patients had their blood pressure controlled compared to 43.5% of those without diabetes (Banegas et al, 2004). A study of 800 hypertensive male veterans in New England reported that blood pressure was less than 140/90 mmHg in only 27% of diabetic persons compared to 34% in those without diabetes (Berlowitz et al, 2003). In a cross-sectional study in Skara Sweden, diabetic patients were more likely to have uncontrolled diastolic blood pressure (DBP) than did non diabetic patients with odds ratio of 2.3(CI 1.3- 4.1) in men and odds ratio of 3.3(1.9- 5.7) in women (Bog-Hansen et al, 2003).

1.5.5 Hyperlipidemia

Hyperlipidemia is defined as an elevation of one or more of cholesterol, cholesterol esters, phospholipids or triglycerides. Data from Framingham Study demonstrate that the risk for developing cardiovascular disease is related to the degree of total cholesterol and LDL-C elevation in a graded continuous manner (Menotti et al, 1996 and Kannel et al, 1996). Hypertensive patients have a greater than expected prevalence of high blood cholesterol levels while conversely patients with hypercholesterolemia have a higher than expected prevalence of hypertension caused by metabolic syndrome. Treatment of hypertension should avoid drugs which can increase cholesterol level, for example diuretics and beta-blockers. Drugs of choice are those that do not affect lipid levels or those that decrease lipids levels (National, Cholesterol, Education, Program, 1994). Hyperlipidemia with or without hypertension is an important predictor of cardiovascular disease (Anderson et al, 1998). All patients should be advised to keep total dietary intake of fat to ≤ 35% of total energy intake, of saturated fats to ≤ 33% of total fat intake, and of cholesterol to < 300 mg / day. Treatment with lipid lowering drugs especially statins, has been shown to reduce cardiovascular morbidity and mortality in patients with a high risk of clinical atherosclerotic disease (Heart Protection Study Collaborative Group, 2002). Studies have found that treatment with lipid lowering drugs in hypertensive patients with hypercholesterolemia have resulted in a significant decrease in blood pressure and this reduction was greater in patients treated with statin (Borghi et al, 2004). Furthermore, in a study of 41 hypertensive patients with hypercholesterolemia, it was found that the use of statin improved blood pressure control (Borghi et al, 2000). In general, patients with

hypercholesterolemia and hypertriglyceridemia were found to have poor blood pressure control (Alkaja et al, 2003). Increased level of low density lipoprotein is associated with poor blood pressure control (Bizien et al, 2004). In fact, total cholesterol of more than 220 mg/dl (5.7mmol/l) was associated with poor blood pressure control as noted by a study of hypertensive patients referred to a nephrology clinic in Italy (Triolol et al, 2004). In a study in a primary care clinic in Sweden, fasting triglycerides levels of ≥ 1.7 mmol/ l was found to be associated with uncontrolled diastolic blood pressure in women (Bøg-Hansen et al, 2003).

1.5.6 Smoking

Smoking is associated with hypertension when it is chronic and heavy (Primatesta et al, 2001). Blood pressure rise acutely during smoking. In a study of 19 smokers with hypertension, blood pressure rose from 140±7/ 99mmHg±3 to 151±5/108±2mmHg within 10 minutes after smoking. Extensive observation data show that smoking has a graded adverse effect on the risk of cardiovascular complications (Doll et al, 1994) and smoking increases CVD risk more than mild hypertension. It is a major factor related to the persistent increase in coronary artery disease and stroke mortality in men with treated hypertension (Anderson et al, 1998). Those who stop smoking experience a rapid decline in risk about 50% after 1year but they need about 10 years to reach the level of non smokers (Rosenberg et al, 1985). Repeated advice from physicians has been shown to decrease smoking by 21% (Law and Tang, 1995). Nicotine replacement therapies can be safely used in hypertensive patients and approximately doubles smoking-cessation rates (Raw et al, 1999). One study found that smoking status doesn't affect blood pressure control but

smokers were given a higher dose of antihypertensive to control their blood pressure (Buhler et al, 1988). Other study report that there was no difference in smoking rates between controlled hypertension and uncontrolled hypertension patients (Joshi et al, 1996). The association between smoking and hypertension control is not very clear as some studies showed a positive relation, while others showed a negative one. Bizien et al (2004) reported good hypertension control among smokers and explained that it was because most smokers were younger and used diuretics more than non smokers did. Another study in the general population of United States showed a low BP control among smokers (He and Muntner 2002). In a study conducted in an inner city hospital, it was found that African American smokers were more likely to have uncontrolled hypertension than did non smokers (McNagny et al, 1997). Additionally, hypertension control was found to be lower among smokers (4.4%) compared to those who never smoked (8.7%) and those who stopped smoking (14.7) (Muntner et al, 2004).

1.5.7 Obesity

Obesity is defined as an excess of body fat or adipose tissue and is often expressed in terms of the body mass index (Lisserner, 1994, Wolf and Colditz 1998). Individuals with a BMI of $\geq$30 kg/m² are considered to be obese (Vanltallie, 1994).

Obese persons have a high risk of developing hypertension and CVD. In a cohort of female nurses, it was found that higher body mass index was associated with an increased risk of hypertension, and women with a body mass index of 31 kg/m² had a multivariate risk of 6.3 compared to women who

had body mass index of less than 20 kg/m² (Huang et al, 1998). In fact, hypertension prevalence among overweight and obese persons is higher than among normal weight persons (Bramlage et al, 2004). Epidemiologic data suggest that obesity contributes to the development of hypertension early in life. In a school survey of children and adolescents, it was found that mean systolic blood pressure increased with an increment in the body mass index (Stephenson, 2003). The medical literature has clearly demonstrated that obesity is an independent risk for a variety of medical conditions, including diabetes mellitus, hypertension, coronary heart disease (CHD) and elevated cholesterol levels (Pi-Sunyer, 1996). Although weight reduction by low-calorie diets have a modest effect on blood pressure in hypertensive obese patients (Conlin et al, 2000 and Svetkey et al, 1999), nearly 50% can expect a reduction of 5/5 mmHg or better in the short term. The BP lowering effect of weight reduction may be enhanced by a simultaneous increase in physical exercise (Neter et al, 2003), by alcohol moderation in heavy drinkers (Puddey et al, 1992) and by reduction in sodium intake (Whelton et al, 1998). A study on hypertensive patients in Japan showed that a higher body mass index (BMI) was associated with lack of systolic hypertension control (Lloyd-Jones et al, 2000). Besides this, another study showed that highest body mass index was associated with poor blood pressure control (Bizien et al, 2004). Finally, another study showed that the odds ratio for good control of hypertension was lower in overweight patients compared to patients with normal weight (0.6 vs. 0.8) (Bramlage et al, 2004).

1.5.8 Sodium intake

Some people are highly sensitive to sodium and this sensitivity can lead to an increase in body fluids leading to an increase in blood pressure. Taking more sodium than needed may increase the blood pressure. In the Dietary Approach to Stop Hypertension (DASH) trial, participants were fed meals with varying salt levels for more than 4 weeks. For both DASH and traditional diets, the lower the salt intake the lower was the blood pressure (Sacks et al, 2002). Salt reduction from an average of 10 to 5g daily lowers BP by about 5/2 mmHg (Whelton et al, 1998) with larger BP falls in the elderly and those with higher initial BP levels (Midgley et al, 1996). Moderate sodium restriction can potentiate the hypertensive effect of many antihypertensive medications (MacGregor et al, 1987). While low sodium diet enhances the antiproteinuric effect of antihypertensive especially ACEIs and ARBs (Houlihan et al 2002, Bakris and Smith 1996). Data from the Third National Health and Nutrition Examination Survey showed that sodium reduction is associated with adequately controlled hypertension (He et al, 2002). This is consistent with the result from a study in China in which salt reduction was associated with hypertension control with an odds ratio of 1.69 (Muntner et al, 2004). This was proven by a study of 114 hypertensive patients in Nigeria which showed that in hypertensive men, the higher the salt intake the higher the blood pressure (Olubodun et al, 1997).

1.5.9 Alcohol consumption

Alcohol intake above 21 unit / week is associated with BP elevation (Hart et al, 1999 and Thun et al, 1997) which is reversible by reducing the intake (Puddey et al, 1992 and Maheswaran et al, 1992). Hypertensive patients should be advised to limit their alcohol intake to 21 units/week for men and 14 units /week for women (William et al, British Hypertension Society Guidelines, 2004). Structured interventions to reduce alcohol consumption have on average a small effect on BP, reducing SBP by about 3 mmHg. In fact, consumption of smaller amounts of alcohol, to the recommended limits, may protect against coronary heart disease (Power et al, 1998).

Alcohol affects hypertension control negatively, this observation was noted in a cross sectional study conducted in Yijing area of Anhui Province in China. It was found that men who drink Chinese liquor (contain 60% alcohol) had higher systolic and diastolic blood pressure than non drinkers (Xu et al, 1997). Another study in China reported that individuals who take equal to or more than two drinks per day were less likely to have controlled blood pressure and that a reduction of alcohol intake was associated with adequate control of hypertension (odds ratio 1.48) (Muntner et al, 2004). Also a cross sectional study in primary care in Spain showed that alcohol consumption was associated with poor control of hypertension (Banegas et al, 2004).

1.5.10 Hyperuricemia

Both animal and human studies have demonstrated that asymptomatic hyperuricemia is associated with the development of cardiovascular disease and is an independent risk factor for the development of hypertension.

Increased uric acid levels in childhood is associated with increased systolic and diastolic pressure and this was also shown in an adult follow up study conducted in Louisiana USA (Alper and Chen et al, 2005). A part from this, the association between blood pressure control and hyperuricemia was also studied in Bahrain in 281 hypertensive patients in primary care centre. It was found that hypertension was poorly controlled in patients with hyperuricemia (Alkaji et al, 2003).

1.5.11 Family history

Patients who develop hypertension before age of 40 years are more likely to have a strong family history. In a screening of more than a half million people, hypertension prevalence in individuals with a positive family history of hypertension was double than that found in individuals with a negative history (Stamler et al, 1979). In a survey among rural residences in the Philippine an association between hypertension and family history was found (Reyes-Gibby and Aday 2000). In a longitudinal study of two samples of 745 subjects (age ranging from 4.9- 27.5 years) and 687 subjects (age ranging from 8.2-27.5) in Georgia in the United States, it was found that subjects with a positive family history of hypertension had higher systolic blood pressure than subjects with a negative family history of hypertension (Dekkers et al, 2003).

Hypertensive patients with family history of hypertension tend to have poor blood pressure control as proven by a study of outpatients in a nephrology clinic in Italy which found that a family history of hypertension was associated with poor control of hypertension (Triolol et al, 2004).

1.5.12 Physical exercise

Taking a regular aerobic exercise has a small effect on blood pressure as it can reduce SBP and DBP by 5-6mmHg (Halbert et al, 2000). In observational studies, it was noted that physical exercise exert a strong protective effect against cardiovascular mortality and this protection is lost when such exercise is discontinued (Sandvik et al, 1993). In fact, experts recommend the performance of mild exercise such as walking for 30-60 minutes at least 3 times a week in order to lower blood pressure (Halbert et al, 1997). Physical exercise was found to be associated with lower systolic and diastolic blood pressure especially in women (Xu et al, 1997). In general, physical exercise is associated with hypertension control (He et al, 2002). Increasing exercise was found to be associated with hypertension control with an odds ratio of 1.66 (Muntner et al, 2004) while a sedentary life style is associated with poor BP control. The latter statement was affirmed by a study in Sweden which found that sedentary life style was associated with isolated uncontrolled systolic hypertension (Bøg-Hansen et al, 2003). Furthermore, another study in Kuwait reported a high sedentary rate of 91.7% in uncontrolled hypertensive patients (Al-Mehza et al, 2004).

1.5.13 Patient compliance

Non-compliance is defined as the failure of the patients to take medications as prescribed by the physician. Many factors can lead to noncompliance like side effects and cost of medications, education levels and knowledge about hypertension. Compliance play an important role in hypertension control as it was found that patient's non compliance was the main cause of uncontrolled

hypertension in many studies, one study in hypertensive patients who received treatment at a cardiology clinic in the Government Medical College in India showed that 61% of those with uncontrolled hypertension did not comply with the prescriptions prescribed. (Joshi et al, 1996).

Some studies also showed that non compliance was also present among patients with controlled hypertension but was generally more among patients with uncontrolled hypertension. A case control study of hypertensive patients indicated that, the rate of compliance was 67% in patients with controlled hypertension compared to 47% in patients with uncontrolled hypertension (Ahluwalia et al, 1997). Furthermore, a survey in Japan reported that noncompliance was found to be higher in patients with poor control of hypertension compared with patients with well controlled hypertension (43% vs. 32%) (Toyoshima et al, 1997).

1.5.14 Patient's knowledge and awareness

Knowledge of individuals about hypertension helps in controlling hypertension, because with this knowledge individuals will visit physician more and adhere to the prescribed treatment. In an interview of 525 hypertensive patients in three heath care centers, poor blood pressure control was found to be associated with a lack of knowledge about the target of systolic blood pressure (Knight et al, 2001). On the other hand, patient's knowledge about hypertension was found to be associated positively with blood pressure control (Majernick et al, 2004). Similarly, Muntner et al (2004) reported that Awareness of hypertension was found to be associated with hypertension control. In the same vein, another study found that patients with low awareness were found to have poor control of

hypertension, this association was especially found to be clear in patients who were 65 years and older, male and those who had not been to see a physician in the previous year (Hyman and Pavlic 2002). Another study showed that a lack of awareness play an important part in poor blood pressure control (Hajjar et al, 2003).

1.5.15 Accessibility to health care

There exist a clear relationship between accessibility to heath care and blood pressure control. This is because patients exposed to health facilities tend to have controlled blood pressure compared with those without health care (Shea et al, 1992). In fact, patients who had a blood pressure measurement during the preceding 6 months or 6- 11 months had better BP control. Another study showed that measuring BP in the preceding 1-5 years was associated with hypertension control (He et al. 2002 and Munter, et al, 2004). Besides this, a case control study of hypertensive patients in outpatient clinics reported that a regular visit to physician during the last 6 months was significantly associated with controlled blood pressure (Ahluwalia et al, 1997). Furthermore, research shows that regular visits to the same health provider and having private insurance was found to be associated with hypertension control (He et al, 2002). In contrast, uncontrolled hypertension was found to be more common in patients who had no primary care physician and who had no health insurance (Saver et al, 1993). Interestingly Paramore et al (2001) found that regular visits to physicians were more common among patients with uncontrolled hypertension.

Access to health care alone is not enough to control hypertension. This indicated by a study on patients with uncontrolled hypertension in The United States, in which it was found that most of those patients had access to health care and frequently visited physicians (Hyman and Pavlik 2000). This seems to imply that physician visit without increasing treatment will not control hypertension. In a study of older men, it was reported that about 40% of patients who had blood pressure of ≥160/90 mm Hg had mean of 6.4± 3.3 hypertension related visits per year. Treatment was increased only in 6.7% of the visits and patients who had more intensive treatment had better blood pressure control than those with less intensive form of treatment (Berlowitz et al,1998).

Finally, uncontrolled hypertension leads to an increased use of health resources in terms of cost of medication and physician visits. In a study of managed care patients with hypertension in New Mexico, it was found that a good relationship exists between medication costs and blood pressure levels i.e. the higher the blood pressure the higher the cost (Paramore et al, 2001).

1.6 Physician factors

Physician attitude toward blood pressure reading is an important factor. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNCVII, 2003) recommended a threshold of 140/90 mmHg to start treatment. Despite this, some physicians adopt a higher than 140/90 mmHg (Hyman and Pavlik 2000). In a study of patients with uncontrolled hypertension, the cut off point for treatment initiation was a diastolic of more than 95 mmHg for 33% of the

physician and a systolic of more than 160 mmHg. In non complicated hypertension, 25% of physicians reported that they would not increase medication if diastolic was 94 mmHg and 33% would not modify treatment if systolic was 158 mmHg. In fact, 41% of physicians said that they were not familiar with JNC guidelines (Hyman and Pavlik 2000).

Physicians tend to delay starting or changing treatment for many reasons. Some believe that diastolic blood pressure is more important than systolic and as such concentrate more on diastolic pressure. Some do not change medication or start treatment until systolic pressure reaches a certain level. Satisfaction with elevated systolic blood pressure is a reason for not intensifying treatment according to a study on primary care in Detroit. This study found that medication change for uncontrolled hypertension occurred only in 38% of the visits. And physicians reported that they would only commence treatment when the systolic blood pressure attained 150 mm Hg and diastolic blood pressure the value reached 91 mm Hg (Oliveria et al, 2002).

Besides this increasing hypertension treatment is not done in many patients with uncontrolled hypertension. In a study conducted in Japan, it was observed that primary care physician increased treatment only in 28% of patients with uncontrolled hypertension and the age of physician was found to be negatively associated with the increased medication prescribed (Asia et al, 2002).

On the other hand, in some settings physicians seem to follow the national guidelines as reported by the authors in a survey of 104 primary care physician