

**EVALUATION OF DOCTORS' ADHERENCE TO MEDICATION
RECOMMENDATIONS OF CLINICAL PRACTICE GUIDELINES
ON MANAGEMENT OF HYPERTENSION (CPG 2008) AT
HOSPITAL PULAU PINANG**

by

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Requirements for the degree of
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(Pharmacy)**

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To

**My precious parents and fiancée Taleeha
who gave me inspiration, unconditional sacrifices and love
for completing this scholastic work**

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LIST OF ABBREVIATIONS

| | |
|--------|---|
| ABB | Alpha beta blockers |
| ACEI | Angiotensin converting enzyme inhibitors |
| AF | Atrial fibrillation |
| ALDA | Aldosterone Antagonists |
| ALLHAT | Antihypertensive And Lipid Lowering Treatment Trial |
| ARB | Angiotensin receptor blockers |
| BB | Beta blockers |
| BHS | British Hypertension Society |
| BP | Blood pressure |
| CAD | Coronary artery disease |
| CCB | Calcium channel blockers |
| CPG | Clinical practice guidelines |
| CHD | Coronary heart disease |
| CHEP | Canadian Hypertension Education Program |
| CHF | Congestive heart failure |
| CKD | Chronic kidney disease |
| COPD | Chronic obstructive pulmonary disease |
| CVA | Cerebrovascular accident |
| CVD | Cardiovascular disease |
| DBP | Diastolic blood pressure |
| DM | Diabetes mellitus |
| EBM | Evidence based medicine |

| | |
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| ESC | European Society of Cardiology |
| ESH | European Society of Hypertension |
| ESRD | End stage renal disease |
| ESRF | End stage renal failure |
| GFR | Glomerular filtration rate |
| HF | Heart failure |
| HPP | Hospital Pulau Pinang |
| HTN | Hypertension |
| IHD | Ischemic heart disease |
| IMPULSION | Implementation of guidelines for the management of arterial hypertension |
| ISH | International Society of Hypertension |
| JNC | Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure |
| LCPGH | Local Clinical Practice Guidelines for Hypertension |
| LVD | Left ventricular dysfunction |
| LVH | Left ventricular hypertrophy |
| MAP | Mean arterial pressure |
| MDRD | Modification of Diet in Renal Disease |
| MI | Myocardial infarction |
| Mm Hg | Millimeter of mercury |
| MREC | Medical Research Ethics Committee |
| NICE | National Institute of Health and Clinical Excellence |
| PVD | Peripheral vascular disease |

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| RENAAL | Reduction of Endpoints in Non-insulin dependent diabetes mellitus with the Angiotensin II Antagonist Losartan |
| SBP | Systolic blood pressure |
| SPSS | Statistical Package for Social Sciences |
| WHO | World Health Organization |
| & | And |

**PENILAIAN KEPATUHAN DOKTOR TERHADAP CADANGAN
PENGUBATAN BAGI PENGURUSAN HIPERTENSI DI DALAM PANDUAN
PRAKTIS KLINIKAL (CPG 2008) DI HOSPITAL PULAU PINANG**

ABSTRAK

Literatur sedia ada menunjukkan salah satu faktor penyumbang utama kepada kawalan buruk hipertensi adalah akibat tidak kepatuhan doktor terhadap panduannya. Penyelidikan ini melibatkan kajian keratan lintang 26 orang doktor di Hospital Pulau Pinang (HPP). Matlamatnya ialah untuk menilai pengetahuan, sikap dan amalan para doktor terhadap panduan praktis klinikal hipertensi Malaysia CPG (2008) dan faktor-faktor yang berkaitan kepatuhan panduan dan kawalan hipertensi. Pengetahuan dan sikap para doktor terhadap CPG (2008) telah dinilai menggunakan satu soal-selidik. Preskripsi yang ditulis oleh 26 orang doktor untuk 650 orang pesakit luar hipertensi (25 preskripsi bagi setiap orang doktor dengan kadar terkeluar kajian 25%) bersama dengan data demografi dan klinikal pesakit telah diperolehi pada lawatan pertama. Preskripsi yang diperolehi dikelaskan kepada samada patuh atau tidak patuh terhadap CPG (2008). Seramai lima ratus dua puluh pesakit (50%) (20 orang pesakit bagi setiap orang doktor telah disusuli untuk satu kali lagi lawatan(kedua). SPSS versi 16 telah digunakan untuk menganalisa data. Satu nilai $p < 0.05$ digunakan sebagai statistik yang signifikan. Berdasar kepada kriteria kesedaran didapati 19 orang doctor (73.07%) mempunyai pengetahuan yang mencukupi berkenaan CPG (2008). Kumpulan yang terdiri daripada pakar dan pakar perunding mempunyai pengetahuan CPG (2008) yang lebih baik daripada pegawai-pegawai perubatan (nilai $p < 0.001$). Doktor bersikap positif terhadap CPG (2008) dengan mata skor purata 23.15 ± 1.34 dan julat mata 19-24 diatas skala mata 30. Korelasi positif yang baik dan signifikan secara statistik diantara pengetahuan doktor

dengan skor praktis telah diperolehi ($r_s=0.635$, nilai $p<0.001$). Tiga ratus empat puluh sembilan pesakit (67.1%) telah menerima farmakoterapi yang komplian terhadap panduan. Analisa multivariat telah mendapati klinik hipertensi sebagai prediktor kuat terhadap ketidakpatuhan panduan (OR=0.398, nilai $p=0.008$). Pada lawatan kedua seramai dua ratus enam puluh lima pesakit (51.0%) telah mencapai matlamat BP. Analisa multivariat telah mendapati perencat penukar enzim angiotensin (OR=2.100, nilai $p=0.001$) dan kepatuhan terhadap panduan (OR=1.745, nilai $p=0.022$) sebagai prediktor kuat kawalan hipertensi sementara penyakit ginjal (OR=0.283, nilai $p<0.001$), diabetes mellitus (OR =0.598, nilai $p=0.025$) dan klinik diabetes (OR =0.384, nilai $p=0.024$) sebagai prediktor kuat bagi kawalan buruk hipertensi. Kajian ini menunjukkan pengetahuan doktor yang mencukupi, kepatuhan CPG (2008) memberikan kawalan baik hipertensi di HPP. Jurang perbezaan diantara cadangan CPG (2008) dengan praktis klinikal telah dapat dilihat dengan jelas dalam farmakoterapi hipertensi yang tidak berkomplikasi, hipertensi dengan diabetes dan penyakit ginjal.

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MANAGEMENT OF HYPERTENSION (CPG 2008) AT HOSPITAL PULAU
PINANG**

ABSTRACT

The existing literature suggests that doctors' divergence from guidelines is one of the major contributing factors for poor control of hypertension. The present research in which 26 doctors were enrolled was cross sectional study conducted at Hospital Pulau Pinang (HPP). Its aim was to evaluate doctors' knowledge, attitude and practice of Malaysian clinical practice guidelines on the management of hypertension CPG (2008), and factors associated with guidelines' adherence and hypertension control. Doctors' knowledge and attitudes on CPG (2008) were evaluated through a questionnaire. Prescriptions written by 26 enrolled doctors to 650 established hypertensive outpatients (25 prescriptions per enrolled doctor with 25% drop out rate) were noted on visit one along with patients' demographic and clinical data. The noted prescriptions were classified either as adherent or non adherent to CPG (2008). Five hundred and twenty (80%) of the enrolled patients (20 patients per enrolled doctor) were followed for one more visit. Blood pressure (BP) noted on visit 2 was related to the prescription written on visit one. SPSS 16 was used for data analysis. A *p*-value <0.05 was considered statistically significant. Nineteen doctors (73.07%) had adequate knowledge of CPG (2008). Group composed of specialists and consultants had significantly better knowledge of CPG (2008) than medical officers (*p*-value <0.001). Doctors were highly positive towards CPG (2008) with mean attitude score of 23.15±1.34 points, ranging from 19-24 points on a 30 point scale. Statistically significant strong positive correlation

($r_s = 0.635$, p -value < 0.001) was observed between doctors' knowledge and practice scores. Three hundred and forty nine (67.1%) patients received guidelines adherent therapy. In multivariate analysis hypertension clinic (OR=0.398, p -value =0.008) was the strong predictor of poor adherence with guidelines. On visit Two, 265 patients (51%) were at goal BP. In multivariate analysis, Angiotensin converting enzyme inhibitors (OR=2.100, p -value=0.001) and guidelines adherence (OR=1.745, p -value=0.022) were the strong predictors of hypertension control, while renal disease (OR=0.283, p -value < 0.001), diabetes mellitus (OR =0.598, p -value =0.025) and diabetic clinic (OR =0.384, p -value =0.024) were the strong predictors of poor control of hypertension. An overall fair to good level of doctors' knowledge, adherence to guidelines and control of hypertension was observed at HPP. The gaps between what CPG (2008) recommended and clinical practice was especially seen in the pharmacotherapy of uncomplicated hypertension and hypertension with diabetes mellitus and renal disease.

CHAPTER 1

INTRODUCTION

1.1 Hypertension

Hypertension is defined as persistently elevated systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood pressure (DBP) of 90 mm Hg or greater (Malaysian Hypertension Guideline Working Group, 2008). Hypertension is usually classified in to two categories:

- a) Essential hypertension, also known as idiopathic or primary hypertension, has no identifiable causes and occurs in 95% of cases (Oparil *et al.*, 2003).
- b) Secondary hypertension, has identifiable causes and occurs in less than 10% of cases (Czarina Acelajado and Calhoun 2010).

1.2 Complications of hypertension

Hypertension is one of the major risk factors for cardiovascular and cerebrovascular diseases (Whelton, 1994). It occurs in isolation in less than 20% cases and is almost always accompanied by other risk factors (Kannel, 2000). By causing electrolyte imbalance, hypertension increases contractile responses, proliferation of the smooth muscle cells, and results in hypertrophy. This hypertrophy contributes to narrowing of the blood vessels and increases the distance required for the diffusion of oxygen from the lumen (Alexander, 1995). Thus causes decrease in partial pressure of oxygen (PO_2), incomplete oxidation, increased free radical concentration, oxidative stress in the arterial wall, tissue damage, and leads to micro and macro-vascular complications (Alexander, 1995). As cardiovascular, cerebrovascular and renovascular systems are involved in

blood pressure regulation, so hypertension causes damage to all of them (Oparil *et al.*, 2003; Beevers *et al.*, 2007).

1.2.1 Hypertension and cardiovascular diseases

Hypertension is one of the major cause of cardiovascular diseases (Lenfant *et al.*, 2003). In population ageing between 40 to 69 years, each increment of 20 mm Hg SBP or approximately equivalent 10 mm Hg DBP is associated with twofold increase in mortality due to stroke, ischemic heart disease (IHD) and other vascular complications (Lewington *et al.*, 2002). The prevalence of congestive heart failure (CHF) was about twofold in hypertensive males as compared to normotensive males, and threefold in hypertensive females as compared to normotensive females (Levy *et al.*, 1996). In a three year follow up study of patients having age more than 65 years, the nonfatal cardiovascular events of myocardial infarction (MI), angina pectoris and heart failure (HF) were significantly correlated with hypertension (Trenkwalder *et al.*, 1999).

1.2.2 Hypertension and diabetes mellitus

Diabetes mellitus and hypertension are strongly interrelated with each other. High prevalence of diabetes mellitus among hypertensive patients has been reported by various studies. In a six-year follow up study, a significant association was found between the onset of diabetes mellitus and the presence of hypertension (Weycker *et al.*, 2009). In a study conducted in Thailand, 78% of diabetic patients were hypertensive (Bunnag *et al.*, 2006). Similarly, 67% of diabetic patients were hypertensive in a study conducted in Malaysia (Chan, 2005). Both hypertension and diabetes in combination alter the endothelial cell structure and function, resulting in vascular complications of

atherosclerosis, nephropathy and retinopathy (Hsueh and Anderson, 1992). Diabetic patients who are already at greater risk of cardiovascular events, the presence of concurrent hypertension results in threefold increase in risk of coronary artery diseases (CAD) and twofold increase in risk of total mortality and stroke (Sowers *et al.*, 2001).

1.2.3 Hypertension and renal disease

Hypertension; both the cause and consequence of renal disease is an accelerating factor for progression of renal failure (Whitworth, 2005). In Reduction of Endpoints in Non-insulin dependent diabetes mellitus with the Angiotensin II Antagonist Losartan (RENAAL) study, increase in baseline SBP was associated with increase in the risk of end stage renal disease (ESRD) or death (Bakris *et al.*, 2003). In Modification of Diet in Renal Disease (MDRD) study, lowering DBP <90 mm Hg decreased the rate of glomerular filtration rate (GFR) decline (Buckalew, 1996). The survival probability of renal function at 10 years decreased with increase in mean blood pressure (BP) among patients with renal disease of different etiologies (Oldrizzi *et al.*, 1993). BP control lowers the progression of end stage renal failure (ESRF) in patients with non diabetic renal disease. Antihypertensive regimens containing Angiotensin converting enzyme inhibitors (ACE inhibitors) are more beneficial in halting the progression of renal disease and improving the rate of GFR (Marcantoni *et al.*, 2000).

1.2.4 Hypertension and cerebrovascular disease

Elevated BP disrupts the auto-regulatory mechanism responsible for smooth and consistent cerebral blood flow, resulting in damage to cerebral blood vessels, thickening of the blood vessel walls, microaneurysmal formation and exposure to stroke (Ogunniyi

and Talabi, 2001). In a population based case control study, after adjustment for confounding factors, strong correlation was observed between the events of stroke and uncontrolled hypertension. Twenty seven percent of the ischemic stroke and 57% of the hemorrhagic stroke was attributed to uncontrolled hypertension (Klungel *et al.*, 2000). Similarly, the relative risk of stroke was greater in patients with uncontrolled hypertension than patients with controlled hypertension (Klungel *et al.*, 1999). In a meta-analysis of 61 observational studies it was observed that mortality rate from stroke was strongly associated with hypertension (Lewington *et al.*, 2002). Results of clinical trials have shown that risk of stroke is clearly reduced by lowering BP (Gueyffier *et al.*, 1997).

1.3 Prevalence, awareness and control of hypertension

Hypertension is a prevalent medical condition in both developed and as well as in developing countries. Nine hundred and seventy two million people around the world were suffering from hypertension in 2000, which is projected to be increase by 60% to a total of 1.25 billion in 2025 (Kearney *et al.*, 2005). Despite its high prevalence, the majority of hypertensive patients are either unaware of their diseased condition; large proportion of the aware population is not on pharmacotherapy and control is suboptimal in those who are on pharmacotherapy (Mohan and Campbell, 2009). According to National Health and Nutritional Examination Survey (NHANES 1999-2004), 29.6% population of the United States suffered from hypertension, and 66.5% of them were aware of their diseased state. Only 53.7% of the aware subjects were on pharmacotherapy and 63.9% of the treated subjects were on goal BP. The overall control rate was 33.1% (Ong *et al.*, 2007). In Netherlands 21.4% males and 14.9% females of

age 30-59 years were hypertensive respectively. Only 17.9% of the hypertensive men and 38.5% of the hypertensive women were on antihypertensive medications. According to Dutch Hypertension Guidelines, 21.9% of the untreated men and 13.6% of the untreated women were eligible for pharmacotherapy (Schelleman *et al.*, 2004).

Hypertension is not a public health problem in the developed world only; the developing countries are also suffering to the same extent. Of the 972 million hypertensive subjects worldwide in 2000; approximately 669 million were from developing world (Kearney *et al.*, 2005). In China, 27.2% of the adult population aged between 35 to 74 years was suffering from hypertension. Less than 45% were aware of their diseased condition, 28.2% of patients were on treatment, and only 8.1% were on goal BP (Gu *et al.*, 2002). Third National Health Examination Survey 2004 of Thailand has reported 22% prevalence of hypertension in population having age ≥ 15 years. Only 31.2% of the hypertensive subjects were aware of their hypertension, 72.8% of the aware patients were on pharmacotherapy and only 36.6% of the treated subjects were on goal BP (Aekplakorn *et al.*, 2008).

Similarly the prevalence of hypertension in Malaysia in subjects having age ≥ 30 years has increased from 32.9% in 1996 to 40.5% in 2004. Only 28.6% of the hypertensive patients who were on antihypertensive therapy were on goal BP (Rampal *et al.*, 2008).

1.4 Factors contributing to suboptimal control of hypertension

According to various guidelines goal BP for uncomplicated and hypertension with various comorbidities is given in table 1.1.

Table 1.1 Goal BP according various hypertension guidelines

| Guideline | Patient assessment | Goal BP (mm Hg) |
|-----------------------|--|----------------------------|
| ESC/ESH (2007) | Uncomplicated hypertension | < 140/90 |
| | Hypertension with comorbidities (Diabetes, CKD, Stroke, MI, Proteinuria) | < 130/80 |
| JNC 7 (2003) | Uncomplicated hypertension | < 140/90 |
| | Hypertension with Diabetes &/or CKD | < 130/80 |
| WHO/ISH (2003) | Uncomplicated hypertension | < 140/90 |
| | Hypertension with Diabetes &/or CKD | < 130/80 |
| CPG (2008) | Uncomplicated hypertension | < 140/85 |
| | Hypertension with Diabetes &/or CKD | < 130/80 |
| | Hypertension with proteinuria ≥ 1 g/24 hrs | < 125/75 |

CKD, chronic kidney disease; MI, Myocardial infarction CPG: clinical Practice Guidelines, ESH/ESC: European Society of Hypertension and European Society of Cardiology; ISH, International Society of Hypertension; JNC 7, Seventh Report of Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; WHO, World Health Organization

Large number of studies has been conducted to identify factors contributing to poor control of hypertension. These factors are arbitrarily classified into patients' related, health care providers' related and system related factors (Borzecki *et al.*, 2005; Ogedegbe, 2008; Wofford and Minor, 2009). Most common patients related factors include non-adherence to medication, medication side effects, pathophysiological causes, age, gender, family history, alcohol intake, knowledge of hypertension, risk factors associated, psychosocial stress etcetera (Borzecki *et al.*, 2005; Ogedegbe, 2008).

Health care provider related factors include clinical inertia, doctors attitudes towards hypertension management, overestimation of the treatment provided, failure to motivate patients to participate in achieving BP goal and constraints of time (Borzecki *et al.*, 2005; Ogedegbe, 2008). System related factors include lack of access to the health care, patient provider interaction and practice setting (Borzecki *et al.*, 2005; Ogedegbe, 2008).

The need to improve hypertension control has initiated the development and dissemination of hypertension management guidelines with the aim to assist health care professionals (Lenfant *et al.*, 2003; Whitworth, 2003).

1.5 Clinical Practice Guidelines

Clinical quality is achieved by developing a system that enhances and optimizes access, multidisciplinary approach, implementation of best practices and patient participation in clinical decision making. Dramatic practice variation observed in clinical practice regarding diagnosis, treatment and prevention of a disease due to uncertainty, biases, and differences of opinions, motives, and values affects clinical quality (Eddy, 1984). In order to change the clinical practice and line up it with evidence based medicine (EBM), multiple strategies including management, regulation and education have been implied (Browman *et al.*, 1995; Woolf *et al.*, 1999). Clinical Practice Guidelines (CPG), defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” (Field and Lohr, 1990) imply all these strategies, and are one the several mechanisms for improving clinical quality (Woolf, 1990).

The objective of CPG is to achieve effective and efficient patient care, educate practitioners, patients and their families, assure and assess quality of care, and guide allocation of health care resources (Tan, 2006). Properly developed guidelines bring EBM into practice; reduce irrational practices, harmful interventions, and make sure the best possible outcomes at the reduced cost (Culleton, 2009).

The delay in implementation of research findings in clinical practice results in suboptimal care of patients. The extreme example of such delay is the use lemon juice for the prevention of Scurvy, which took 50 years for British Navy and 120 years for Merchant Marine to practice it after the discovery (Haines and Jones, 1994). It is found that on average it takes 17 years to integrate the facts found in a clinical trial into clinical practice, and even then the evidence is not incorporated in systematic way (Carroll 2002). The effective and systematic way of bringing and practicing these evidences in to clinical practice is the development and dissemination of CPG (Grimshaw *et al.*, 2005).

Clinical practice guidelines which were initially mainly based on expert opinions of “opinion leaders” are now considered to be evidence based and systematically developed (Lohr *et al.*, 1998). Clinical practice guidelines should be valid, reliable, clinically applicable and flexible, explicit, developed through multidisciplinary process, continuously updated and documented (Field and Lohr, 1990; Tan, 2006). The skills and resources required for the development of CPG are usually not available to individuals or a single health care organization, due to this reason CPG are developed by specialized national and international institutions (Ollenschläger *et al.*, 2004).

1.5.1 Impact of Clinical Practice guidelines on patient outcomes

Large number of CPG are developed, widely disseminated and regularly updated in almost every field of medicine including both physical and mental health. For improving the delivery of quality of care to achieve best possible outcomes, the systematic dissemination and successful implementation of the guidelines is of utmost importance (Lugtenberg *et al.*, 2009).

Existing literature suggests that most of the time successful implementation of guidelines has resulted in improved quality of care and patient outcomes. For example, successful implementation of the guidelines developed by Dutch College of General Practitioners on the management of asthma and chronic obstructive pulmonary disease (COPD) resulted in significant improvements in lung functions and respiratory symptoms (Jans *et al.*, 2001). In a multi-centre observational study conducted in six European countries France, Germany, The Netherlands, Italy, Spain and UK, adherence to the European guidelines on management of CHF was strongly and independently correlated with fewer CHF and cardiovascular hospitalization rates (Komajda *et al.*, 2005). Hypertension control was significantly better in high risk cardiovascular patients treated by group of physicians who had received specific training European Society of Hypertension (ESH) guidelines (Asmar *et al.*, 2007). Ansari *et al.*, 2003 while conducting a retrospective cohort study on new onset heart failure (HF) outpatients found that adherence to guidelines was the only predictor of reduction in mortality and cardiovascular hospitalization.

In Implementation of guidelines for the management of arterial hypertension (IMPULSION) study, a notable improvement was seen in achieving BP goal (Karagiannis *et al.*, 2009). Positive outcomes of CPG implementation on the control of hypertension was seen in a study conducted at Kyushu University Hospital (Ohta *et al.*, 2004). Similar promising results regarding improvement in quality of care and control of hypertension were observed after the implementation Local Clinical Practice Guidelines for Hypertension (LCPGH) in a study conducted in Kuwait (Al-Awadhi *et al.*, 2007).

Findings of these studies suggest that guidelines have the potential to improve quality of care and achieve best possible patient outcomes.

1.5.2 Clinical practice guidelines and management of hypertension in clinical practice

In order to improve hypertension control, reduce practice variation and provide cost beneficial therapy a large number of guidelines for the management of hypertension has been developed and disseminated in various countries around the world. Various major guidelines for management of hypertension include World Health Organization/International Society of Hypertension Guidelines on Management of Hypertension (WHO/ISH 2003), Guidelines for the Management of Arterial Hypertension of the European Society of Hypertension and the European Society of Cardiology (ESH/ESC 2007), Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7) , British Society of Hypertension Guidelines (BSH 2004) and Canadian Hypertension Education Program (CHEP 2009). Ministry of health Malaysia in collaboration with, Malaysian Society of Hypertension and Academy of Medicine is also developing and disseminating guidelines for the management of hypertension since 1998. The latest version of Malaysian clinical practice guideline on management of hypertension CPG (2008) is issued in 2008.

Despite the availability and dissemination of hypertension management guidelines, literature review suggests the existence of a wide gap between guidelines recommended and actual clinical practices. While managing hypertension, almost the same problems

and deviation from the guidelines recommended practices are observed in each country, namely, insufficient diagnostic work (Cuspidi *et al.*, 2002; Spranger *et al.*, 2004; Marija *et al.*, 2007) setting a high threshold BP levels than recommended (Berlowitz *et al.*, 1998; Oliveria *et al.*, 2002; Jafar *et al.*, 2005; Redón *et al.*, 2010), poor evaluation and recording of cardiovascular risk factors (Langham *et al.*, 2002; Sheerin *et al.*, 2007), insufficient patient counseling on non pharmacological interventions (Hobbs and Erhardt, 2002; Odili *et al.*, 2008), and prescription of antihypertensive agents other than recommended (Monane, *et al.*, 1995; Siegel and Lopez, 1997; Knight *et al.*, 2000; Chan, 2005; Drawz *et al.*, 2009; Ramli *et al.*, 2010).

Pharmacotherapy is one of the main stay of hypertension management. On the basis of evidences obtained from clinical trials, guidelines have recommended various antihypertensive classes as preferred agents for treating hypertension with and without compelling indications. Initial choice of therapy recommended by various hypertension guidelines in various conditions is given in table 1.2

Table 1.2 Preferred antihypertensive agents by various guidelines in patients with and without compelling indications

| Guideline | Patient assessment | Initial Drug choices |
|----------------------------------|---|--|
| JNC 7 | No compelling indication | Thiazide Diuretics (for most patients) |
| | Diabetes mellitus | ACEI, ARB |
| | Chronic kidney disease | ACEI , ARB |
| | Stable angina pectoris | BB (for most) alternatively CCB can be used |
| | Unstable angina or myocardial infarction | BB, ACEI |
| | Post myocardial infarction | ACEI, BB, Aldosterone Antagonists |
| | Asymptomatic heart failure with demonstrable ventricular dysfunction | ACEI, BB |
| | Heart failure with symptomatic Ventricular dysfunction or end stage heart disease | ACEI, BB, ARB, Aldosterone Antagonists along with Loop diuretics |
| WHO/ISH guidelines (2003) | No compelling indication | Thiazide diuretics (for most patients) |
| | Diabetic nephropathy type 1 | ACEI |
| | Diabetic nephropathy type 2 | ARB |
| | Non diabetic nephropathy | ACEI |
| | Post myocardial infarction | ACEI, BB |
| | Left ventricular dysfunction | ACEI |
| | Congestive heart failure | Diuretics almost always included, BB, Spironolactone |
| | Left ventricular hypertrophy | ARB |
| | Cerebrovascular disease | ACEI, Diuretic |
| | Elderly with Isolated systolic hypertension | Diuretic, Dihydropyridine CCB |

“Table 1.2 continued”

| | | |
|-----------------------------|--|---|
| Malaysian CPG (2008) | No compelling indication | ACEI,ARB,CCB,Diuretics |
| | Diabetes mellitus without proteinuria | ACEI |
| | Diabetes mellitus with proteinuria | ACEI, ARB |
| | Chronic kidney disease | ACEI |
| | Coronary heart disease | BB, ACEI, long Acting CCB |
| | Coronary heart disease with post myocardial infarction and/or left ventricular dysfunction | BB, ACEI, Aldosterone antagonists |
| | Heart failure | Diuretics, ACEI, BB, ARB, Aldosterone antagonists |
| | Left ventricular hypertrophy | ARB |
| | Primary prevention of Stroke | CCB |
| | Secondary prevention of stroke | ACEI, ARB |
| | Elderly with isolated systolic hypertension | Diuretics |

ACEI, Angiotensin converting enzyme inhibitor; ARB, Angiotensin receptor blocker; BB, Beta blockers; CCB, Calcium channel blockers; CPG, Clinical practice guidelines; ISH, International Society of Hypertension; JNC 7, Seventh Report of Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure; WHO, World Health Organization

Despite evidence based pharmacotherapeutic recommendations, doctors are found to deviate from guidelines while prescribing antihypertensive drugs. For example, in a study conducted at a nursing home in United States of America (USA), only 18% of uncomplicated hypertensive patients received JNC 7 recommended therapy. The majority of patients to whom Thiazide diuretics should have been prescribed were on BB, ACE inhibitors, CCB and ARB (Drawz *et al.*, 2009). Guidelines divergent antihypertensive prescribing trend was observed in a study conducted in Taiwan. More than half of the patients were on monotherapy. Among all of the monotherapy, CCB were the highly prescribed drugs, prescribed to 33.5% patients, followed by BB. guidelines recommended diuretics made only 8.3% of the whole monotherapy (Pang-Hsiang and Jung-Der, 2008). Similarly only 50% of the essential hypertensive patients were on the JNC 6 recommended diuretics and BB, and 51.3% of the diabetic hypertensive patients were on diuretics and CCB rather than the JNC 6 recommended ACE inhibitors (Holmes *et al.*, 2004). In a study conducted in USA, CCB and ACE inhibitors were the most commonly prescribed antihypertensives to elderly patients rather than guidelines recommended Thiazide diuretics and BB (Knight *et al.*, 2000). Similar findings were observed in another study conducted in USA, which concluded that the antihypertensive prescribing practices from 1992 to 1995 were not in accordance with JNC V guidelines, where decrease in prescription of guidelines recommended Thiazide diuretics and BB was observed (Siegel and Lopez, 1997).

Similar scare and poor adherence to hypertension guidelines was observed in studies conducted in Malaysia. A cross sectional study conducted at 11 health care clinics in Melakah has reported that only 3.1% of the diabetic hypertensive patients were on goal

BP. One hundred and thirty four of the uncontrolled hypertensive patients were not on antihypertensive therapy and only 18.3% of the diabetic hypertensive patients were on the CPG (2002) recommended ACE inhibitors (Chan, 2005). Due to accumulating evidence that the use of BB is associated with significant increase in stroke (Lindholm *et al.*, 2005) and cardiovascular events in elderly patients (Khan and McAlister, 2006), Malaysian CPG (2008) has discouraged the use of BB as initial agents for treating uncomplicated hypertension. Despite the discouragement by CPG (2008), BB were reported the most commonly prescribed drug in the form of mono as well as combination therapy in a study conducted in Malaysia (Ramli *et al.*, 2010).

1.6 Adherence to clinical practice guidelines

The findings of abovementioned studies indicate the existence of a large discrepancy between the guidelines recommendations and management of hypertension in clinical practice. There are several models which discuss the process and factors leading to guidelines adherence.

1.6.1 Awareness to Adherence Model

Implementation of guidelines in clinical practice is not a straight forward process. Various strategies are adopted for its implantation. These strategies include diffusion, dissemination and implementation. After concluding that Passive Dissemination Model (a model based on assumption that targeted audience specific communication of the guidelines will affect and change their behavior) is over-simplistic, Pathman and his colleagues proposed a model known as Awareness to Adherence Model to explain the process resulting in adherence to guidelines (Pathman *et al.*, 1996).

Pathman model is a phase model consisting of four steps that is awareness, agreement, adoption and adherence. According to the model, for performing a behavior or adhering with a practice, first of all it is necessary to become aware of the practice (awareness), then agree with it (agreement), then decide to follow it (adoption) and at last following it in the practice successfully (adherence) (Pathman *et al.*, 1996). This model is based on Trans-theoretical Model of change, which consists of five stages, pre-contemplation, contemplation, action, maintenance and relapse. According to Trans-theoretical model the individual takes change intentionally after becoming aware of the pros of change and cons of former behavior (Prochaska and DiClemente, 1983).

Although the study conducted by Pathman *et al.*, 1996 supported his model, but still 11% doctors adhered with Hepatitis B vaccine's recommendation without being agree with it. Support for Awareness to Adherence model is reported by a study conducted in UK. The model was evaluated for recommendations of British Hypertension Society (BHS) and National Institute of Health and Clinical Excellence (NICE) guidelines. It was observed that model was not applicable only to 6-8% of the doctors' responses, but a larger discrepancy of 15% to 19% was observed for the recommendations for which respondents were receiving financial incentives. The doctors reported adherence to guidelines recommended practices without being expressing awareness or agreement (Heneghan *et al.*, 2007). In another study it is found that although awareness, agreement and adoption were the strongest predictors of adherence to guidelines recommendations, the adoption rate varied even among the doctors who were familiar with the recommendations. Thus suggesting practical obstacles other than awareness to the implementations of guidelines (Beaulieu *et al.*, 2005).

1.6.2 Cabana Model

An alternative model of guidelines adherence is proposed by Cabana and his colleagues (Cabana *et al.*, 1999). After conducting a review of 76 studies, examining barriers to guidelines adherence, they found that factors related to knowledge, attitude and behavior act as barriers to guidelines adherence. According to the model, barriers limiting adherence to guidelines are classified into three categories:

1.6.2 (a) Knowledge related factors

These include factors which limit guidelines adherence through cognitive components such as lack of awareness and familiarity.

1.6.2 (b) Attitude related factors

These include factors which limit guidelines adherence through affective component such as lack of agreement, lack of outcome expectancy, self efficacy and motivation.

1.6.2 (c) Behavior related factors

These include factors which limit guidelines adherence by restricting doctors' ability such as characteristics of patients, guidelines and practice.

This model suggests a sequential process of behavior change, that is, guidelines first affect doctors' knowledge, then attitude before changing their behavior. Although behavior can be changed without changing knowledge and attitude but that change is not long lasting (Cabana *et al.*, 1999).

1.7 Factors affecting guidelines adherence

1.7.1 Doctors' knowledge or familiarity with guidelines

Doctors' adherence to guidelines is repeatedly linked to their familiarity with guidelines, which is considered to be the first step to implement them in clinical practice (Pathman *et al.*, 1996; Cabana *et al.*, 1999; Windak *et al.*, 2007). It is found that doctors who were more familiar with the guidelines remained more adhere to them (Cheng *et al.*, 1996; Hyman and Pavlik, 2000; Nelson *et al.* 2003; Ikeda *et al.* 2005; Petek Šter and Kersnik, 2005; El-Solh *et al.*, 2010).

However this relationship between doctors' knowledge and adherence to guidelines does not necessarily follow the same sequence always. For example in a study only, 51.8% doctors were using guidelines occasionally or always, despite the fact that all of them were well aware of guidelines' recommendations (Wang and Wang, 2004). Similar poor adherence to JNC 7 guidelines was noted among doctors 94% of whom were familiar with its recommendations (Holland *et al.*, 2008).

1.7.2 Doctors attitudes toward guidelines

Attitudes refer to feelings as well as preconceived ideas towards a particular subject (Kaliyaperumal, 2004). Doctors' attitudes towards guidelines play a significant role in their implementation in clinical practice (Cabana *et al.*, 1999). Doctors' intentions to use the guidelines can be predicted from their attitudes towards them (Limbert and Lamb, 2002) which are influenced by many factors, such as their knowledge, past clinical experience, beliefs about guidelines, outcome expectations, peers' opinions and

guidelines characteristics (Tan, 2006). Doctors' positive attitudes towards guidelines were associated with adherence to guidelines and vice versa. (Merritt *et al.*, 1999; Subramanian, *et al.* 2004; Beaulieu *et al.*, 2005; Haagen *et al.*, 2005; Quiros *et al.*, 2007).

1.7.3 Doctors demographics

Beside knowledge and attitudes, doctors demographics were also been tied to guidelines adherence. Doctors' age (Nelson *et al.*, 2003; Holmes *et al.*, 2004; Ikeda *et al.*, 2005), gender (Nichol and Zimmerman, 2001; Broder *et al.* 2005; Skelding *et al.*, 2006), specialty and experience (McAlister *et al.*, 1997; Fams *et al.*, 2002; Cuspidi *et al.*, 2003; Schaars *et al.*, 2004) were also reported to had association with guidelines adherence.

1.7.4 Practice setting characteristics

According to Cabana *et al.*, 1999 in addition to knowledge and attitudes other contextual variables like implementation strategy, practice characteristics, opinion leaders, and audit of the practices also affect adherence to guidelines. For example placing written, verbal and computer based reminder tools at practice setting increased guidelines adherence (Weingarten *et al.*, 1994; Goethe *et al.*, 1997). In a qualitative study the respondents cited structural barriers like work load, lack of ready access to protocols, inadequate computerization and lack of audit on practices as reasons for nonadherence to hypertension guidelines (Cranney *et al.*, 2001). Similarly, lack of appropriate supportive staff, financial constraints, work and information overload, lack of training and audit of physicians' practices, and influence of local consultants were contributing factors for non adherence to guidelines (Hobbs and Erhardt, 2002; Rashidian *et al.*, 2008).

1.7.5 Patients' factors

In addition to doctors and system related factors, some studies have found relationship between doctors' adherence to guidelines and patients' factors like age, gender, ethnicity, insurance status, comorbidities etcetera. Studies have reported mixed results in this regard. In a study it is observed that male gender was associated with receiving guidelines recommended antihyperlipidemic drugs in patients at high risk for cardiovascular diseases (Graversen *et al.*, 2010). In another study female gender was found to be associated with receiving guidelines recommended therapy as compared to male patients (Holmes *et al.*, 2004; Skelding *et al.*, 2006). Guidelines recommended hypertension management was significantly associated with patients minority status (non white), total comorbidities, CAD, history of myocardial infarction, history of stroke, diabetes and number of medications (Arderly *et al.*, 2007). Some studies had not found any relationships between the patients' characteristics and doctors' adherence to guidelines (Russell *et al.*, 2005; Wae *et al.*, 2006).

1.8 Conceptual Frame work

The above discussion regarding poor control of hypertension can be simply summed up in Fig 1.1

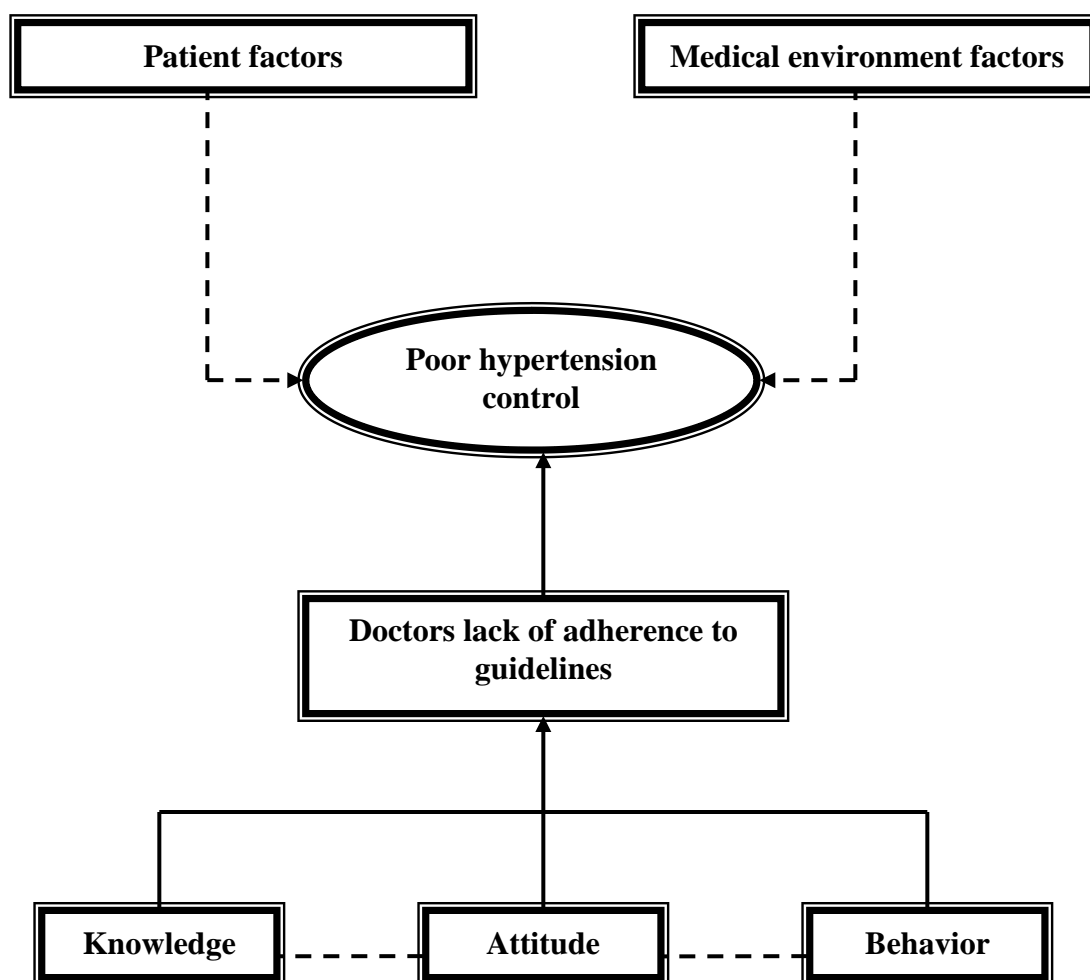


Fig 1.1 Factors contributing to poor control of hypertension

1.9 Measuring adherence to hypertension guidelines

Various strategies are used to evaluate doctors' adherence to hypertension guidelines.

These strategies include:

- i. Antihypertensive prescription data and prescribing trends over the time
- ii. Survey conducted via a questionnaire
- iii. Revision of patients' medical record

1.9.1 Evaluation of guidelines adherence by utilizing prescription data and prescribing trends over the time

Using prescription data and prescribing trends over the time is one of the main strategies used for evaluating doctors' adherence to hypertension guidelines. Different conclusions have been drawn by these studies. Basic features of the studies which had used this strategy are given in table 1.3.

Table 1.3 Basic features of the studies which has evaluated guidelines adherence by evaluating prescription data and prescribing trends over the time

| Study | Evaluation of comorbidities | Evaluation of justified non adherence | Related adherence to hypertension control | Conclusion |
|-----------------------------------|------------------------------------|--|--|--|
| (Monane <i>et al.</i> , 1995) | No | No | No | Prescribing practices were not in line with guidelines |
| (Siegel and Lopez, 1997) | No | No | No | Prescribing practices were not in line with guidelines |
| (Nelson and Knapp, 2000) | No | No | No | Prescribing practices were in line with guidelines |
| (Knight <i>et al.</i> , 2000) | Yes | No | No | Prescribing practices were not in line with guidelines |
| (Siegel <i>et al.</i> , 2001) | No | No | No | Prescribing practices were not in line with guidelines |
| (Campbell <i>et al.</i> , 2003) | No | No | No | Prescribing practices were in line with guidelines |
| (Hemmelgarn <i>et al.</i> , 2008) | No | No | No | Prescribing practices were in line with guidelines |
| (Pang-Hsiang and Jung-Der, 2008) | Excluded | No | No | Prescribing practices were not in line with guidelines |
| (Drawz <i>et al.</i> , 2009) | Excluded | Yes | No | Prescribing practices were not in line with guidelines |

1.9.1 (a) Limitations

- i) Except the studies conducted by Knight *et al.*, 2000 and (Pang-Hsiang and Jung-Der, 2008; Drawz *et al.*, 2009) in which comorbidities were included and excluded respectively, none of the above studies have addressed comorbidities, an important consideration while evaluating guidelines adherence (Carter *et al.*, 2000).
- ii) The majority studies have not defined explicit criteria for guidelines adherence.
- iii) Except the study conducted by Drawz *et al.*, 2009, rest of them failed to conduct the detailed review of patients' medical record to find whether the divergence from guidelines was justifiable or not.
- iv) None of the above studies correlated practices to hypertension control, this limitation made these studies somewhat non conclusive.

1.9.2 Evaluation of guidelines adherence by using doctors' survey data

Survey data have been used by various researchers to evaluate doctors' familiarity with hypertension guidelines. These studies were based on the hypothesis that doctors' poor familiarity about hypertension guidelines is a major reason for guidelines divergent practices. Different conclusions have been drawn by these studies. Basic features of these studies are given in table 1.4.