

“CLINICAL AND LABORATORY PROFILE OF  
PREHYPERTENSION IN ADULTS – A ONE  
YEAR CROSS SECTIONAL STUDY”

REG NO. BG0108006

Dissertation

Submitted to the  
KLE University, Belgaum, Karnataka

In Partial Fulfillment  
of the requirements for the degree of

M. D.  
in  
GENERAL MEDICINE

**DEPARTMENT OF GENERAL MEDICINE,  
JAWAHARLAL NEHRU MEDICAL COLLEGE,  
BELGAUM, KARNATAKA**

**MAY - 2011**

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**ENDORSEMENT BY HOD, PRINCIPAL**

This is to certify that the dissertation entitled  
**“CLINICAL AND LABORATORY PROFILE OF  
PREHYPERTENSION IN ADULTS – A ONE YEAR  
CROSS SECTIONAL STUDY”** is a bonafide research work  
done by **THE CANDIDATE REG NO. BG0108006** in the  
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## LIST OF ABBREVIATIONS USED

%	-	Percentage
(Delta)	-	Change in blood pressure
ACR	-	Albumin / creatinine ratio
ADA	-	American Diabetes Association
Ang	-	Angiographic
ARB	-	Angiotensin Receptor Blocker
ARIC	-	Atherosclerosis Risk In Communities
ATP	-	Adult Treatment Panel
AVIATOR	-	Aliskiren in Visceral Obesity at Risk Patients Outcomes Research
BHR	-	Basal heart rate
BMI	-	Body mass index
BP	-	Blood pressure
CAD	-	Coronary artery disease
CARDIA	-	Coronary Artery Risk Development In young Adults
CHD	-	Coronary heart disease
Cms	-	Centimeters
CV	-	Cardiovascular
CVD	-	Cardiovascular disease
DASH	-	Dietary approaches to stop hypertension
DBP	-	Diastolic blood pressure
DM	-	Diabetes mellitus
GFR	-	Glomerular filtration rate
HDL	-	High density lipoprotein

HR	-	Heart rate
HsCRP	-	High sensitivity C-reactive protein
IHD	-	Ischaemic heart disease
IPD	-	In patient department
JNC	-	Joint National Committee on Prevention, Detection, Evaluation and Treatment of high Blood pressure
LDL	-	Low density lipoprotein
LV	-	Left ventricle
mm Hg	-	Millimeter of mercury
MONICA	-	Monitoring Of Trends and Determinants In Cardiovascular Disease in Augsburg Cooperative research in the region of Augsburg study
NHANES	-	National health and nutritional examination survey
NHBPEP	-	National high blood pressure education program
NHEFS	-	NHANES I Epidemiologic follow up study
OPD	-	Out patient department
PILL	-	Program to Improve Life and Longevity
PR	-	Pulse rate
PreHTN	-	Prehypertension
RR	-	Relative risk
SBP	-	Systolic blood pressure
TG	-	Triglycerides
TMT	-	Tread mill test
TROPHY	-	Trial of Preventing Hypertension
US	-	United States

WHI - Women Health Initiative  
WHR - Waist Hip Ratio

## **ABSTRACT**

### **Background and objectives**

This is era of pandemic of prehypertension. Prehypertension is defined as BP in the range of 120 to 139 mm Hg (in systole) or 80 to 89 mmHg (in diastole). It is associated with many risk factors such as sympathetic overactivity, abnormal lipid profile, obesity and diabetes. Prevention of prehypertension is important goal for primary care patients. Objectives of present study were to evaluate clinical and laboratory profile of prehypertensives.

### **Methodology**

Present one year cross sectional study was conducted in Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 100 patients with prehypertension during period of January 2009 to December 2009. Demographic data with relevant history was collected and thorough clinical examination was conducted. Three BP readings, five minutes apart were taken and mean of second and third reading was selected as final blood pressure. Special tests such as renal function tests, Lipid Profile, Tread Mill Test and fundoscopy were conducted and recorded.

### **Results**

Majority of study participants were males (83%) and aged between 41 to 50 years (39%) followed by 51 to 60 years (33%). Majority (61%) patients were overweight and obese, with overall mean basal heart rate of  $82.50 \pm 10.37$  beats/min and 28% were diabetics. Angiographic CAD probability calculated by simple exercise test score showed majority (61%) having; intermediate (46%)

and high (15%) probability. TMT was positive for inducible ischaemia in 13% subjects. Hypertensive BP response was seen in 16% subjects. Heart rate recovery time, marker of autonomic dysfunction was blunted in 5% of prehypertensives.

### **Conclusion**

Age, smoking, family history, prediabetes and diabetes are important risk factors for prehypertension. Obesity, dyslipidemia and basal heart rate of more than 80 beats/min formed an important risk factors, as well as determinants of prehypertension. Prehypertensives are at increased risk for cardiovascular disease and progression to hypertension.

### **Key words**

Diabetes mellitus; Prediabetes; Prehypertension; Tread Mill Test;

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## **INTRODUCTION**

Prehypertension was introduced by the Seventh Report of the Joint National Committee (JNC-7) on the prevention, detection, evaluation and treatment of High Blood Pressure in 2003.<sup>1,2</sup>

Prehypertension is defined as blood pressure (BP) in the range of 120 to 139 mm Hg (in systole) or 80 to 89 mmHg (in diastole), which was termed as ‘normal blood pressure’ or ‘high-normal blood pressure’ in the JNC-6 report.<sup>3</sup>

The new term prehypertension was based on a number of epidemiological studies. Several studies have shown that BP increases with age, and in Framingham Heart Study, about 90% of those whose BP was normal at age 55 years ultimately developed hypertension in their lifetime.<sup>4</sup> A meta-analysis of the individual data for one million adults in 61 prospective studies showed that the risk of cardiovascular disease (CVD) increased progressively from levels as low as 115/75 mmHg, and each increment of 20/10 mmHg is associated with more than a twofold difference in the stroke death rate and a twofold difference in the death rates from ischemic heart disease (IHD) and from other vascular causes.<sup>5</sup>

After this data was published, there is a need to alert those individuals with BPs above this level about their high cardiovascular risk. Therefore, the introduction of the new term prehypertension was appropriate and well-timed. Prehypertension focuses on a population who were previously called “High-normal BP”. The recent data has shown the prevalence of prehypertension and its

progression to hypertension, its association with CVD risk factors and its relationship with the development of CVD.

The risk of CV events in prehypertension lies between normotension and hypertension. A 10 mm Hg lower usual SBP or 5 mm Hg lower usual DBP would be associated with about 40% lower risk of stroke death and about 30% lower risk of death from IHD or other vascular causes throughout middle to old age. So, for the general normotensive population, producing persistent reductions in the average blood pressure of just a few mmHg should avoid large numbers of premature deaths and disabling strokes.<sup>5</sup> The treatment recommendations are still lifestyle modification. To introduce pharmacologic treatment into the present treatment paradigm is yet a new challenge.

It is estimated that 31% of the US population and 29% of the Korean population have prehypertension.<sup>6</sup> In India, a study conducted in Chennai has reported 47.4% prevalence of prehypertension.<sup>7</sup> This condition is very prevalent and it is associated with other cardiovascular risk factors, especially smoking, obesity and diabetes. These people are at high risk for developing hypertension and subsequent cardiovascular events. Therefore, prehypertension has become a major public health concern. Prehypertension is an important entity which is widely prevalent and not much attention has been paid to it.

Prevention of prehypertension is important goal for primary care patients. It is associated with many risk factors such as sympathetic overactivity, abnormal lipid profile, obesity, diabetes and coronary artery disease.

Heart rate  $> 80$  in prehypertensives is also found to be associated with increased overall mortality and increased CHD risk but very little data is available to establish the fact especially in Indian context.<sup>8</sup>

Hence the present study is aimed to establish correlation between prehypertension and various other facts like obesity, diabetes, cardiovascular disorders and target organ damages.

## **OBJECTIVES**

The objectives of the present study were to evaluate clinical and laboratory profile of prehypertensives.

## **REVIEW OF LITERATURE**

The Seventh Report of the Joint National Committee (JNC-7) introduced a new term “prehypertension”.<sup>1,2</sup> This condition is very prevalent and it is associated with other cardiovascular risk factors, especially obesity and diabetes. These people are at high risk for developing hypertension and subsequent cardiovascular events. Therefore, prehypertension has become a major public health concern, but the treatment standards have not yet been established. The JNC-7 report has recommended healthy lifestyles for all the people with prehypertension and it especially advocated drug treatment for the group of people with diabetes or chronic renal disease.

### **History**

Some cite the writings of Sushruta in the 6th century BC as being the first mention of symptoms like those of hypertension. Others proposed even earlier descriptions dating as far as 2600 years before Christ. Main treatment for what was called the "hard pulse disease" consisted in reducing the quantity of blood in a subject by the sectioning of veins or the application of leeches. Well known individuals such as The Yellow Emperor of China, Cornelius Celsus, Galen, and Hipocrates advocated such treatments.

The concept of blood pressure was known to our ancestors, many centuries before Christ. History of blood pressure measurement goes back to Stephen Hales (1773), who measured the intra-arterial pressure by the direct

method in man. He observed that blood exerts a pressure and circulation obeys the other hydrostatic laws.

In 1828, Jean Poiseulle devised the mercury manometer for measuring blood pressure and Harrison in 1883 modified it and was able to measure arterial pressure by crude method on intact vessels. But the credit goes to Riva Rocci who devised the acceptable sphygmomanometer, with a circular compression of upper arm with a 5 cm wide rubber bag in 1896, which became the forerunner of modern sphygmomanometer.

The modern concept of auscultatory method of recording blood pressure was land marked in blood pressure history by Korotkoff in 1904 who described five distinct phases of sound heard with stethoscope.

Although induration of the kidney with oliguria, hematuria, and oedema has been known for more than 1000 years, it remained for Richard Bright in 1827 to associate the clinical findings of albuminuria, hardness and fullness of pulse and left ventricular hypertrophy with the pathological finding of sclerosing and contracted kidney and he first originated the concept of arterial hypertension with the kidney.

A prominent victim of severe hypertension leading to cerebral hemorrhage was Franklin D. Roosevelt (1882–1945). The Framingham Heart Study added to the epidemiological understanding of hypertension and its relationship with coronary artery disease.<sup>9</sup>

## **Prehypertension**

The term prehypertension was coined in 1939 from a study which observed that blood pressure measurements greater than 140/90 mm Hg were associated with a sharp increase in mortality compared with lower measurements, giving rise to the usual clinical definition of hypertension.<sup>10</sup> In addition, systolic blood pressure in the range 120–140 mm Hg, especially when occurring in younger individuals, was associated with progression to definitive hypertension and cardiovascular disease later in life. Individuals with prehypertension have increased mortality rates that are directly proportional to blood pressure.

60 years later, the concept of prehypertension was promulgated into guidelines for the management of blood pressure by the seventh report of the Joint National Committee on Prevention, Detection, evaluation, and treatment of High Blood Pressure.<sup>1,2</sup>

Prehypertension was introduced by the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) in 2003.<sup>1,2</sup>

## **Definition**

Prehypertension was defined as a systolic blood pressure of 120–139 mm Hg and/or a diastolic blood pressure of 80–89 mm Hg. The objectives of creating this blood pressure classification were to increase awareness of the importance of identifying individuals in whom early intervention by adoption of healthy lifestyles could lower blood pressure, decrease the rate of progression to

hypertensive levels, or to prevent hypertension entirely and thereby reduce risk of cardiovascular disease.<sup>1,2</sup>

### **Need For Such Terminology**

Prehypertension is defined as blood pressure (BP) in the range of 120-139 mm Hg (in systole) or 80-89 mm Hg (in diastole), which was termed as 'normal blood pressure' or 'high-normal blood pressure' in the JNC-6 report. The new term prehypertension was based on a number of epidemiological studies. Several studies have shown that BP increases with age, and in Framingham Heart Study, about 90% of those whose BP was normal at age 55 years ultimately developed hypertension in their lifetime.<sup>4</sup> A meta-analysis of the individual data for one million adults in 61 prospective studies showed that the risk of cardiovascular disease (CVD) increased progressively from levels as low as 115/75 mm Hg, and each increment of 20/10 mm Hg is associated with more than a twofold difference in the stroke death rate and a twofold difference in the death rates from ischemic heart disease (IHD) and from other vascular causes.<sup>5</sup> After this data was published, there is a need to alert those individuals with BPs above this level about their high cardiovascular risk. Therefore, the introduction of the new term prehypertension was appropriate and well-timed.

The impetus for creating the prehypertension blood pressure category came, at least in part, from a metaanalysis that included approximately 1 million individuals from 61 longterm epidemiological studies. The metaanalysis demonstrated that mortality from ischemic heart disease and stroke in individuals

aged 40–89 years increases in a log linear relationship together with increases in both systolic and diastolic blood pressure.

Furthermore, longitudinal data from the Framingham Heart study indicated that individuals formerly classified as having ‘normal’ and ‘highnormal’ blood pressure (120–139/80–89 mm Hg) are at increased risk of developing fullblown hypertension and cardiovascular disease later in life than those who have an optimal blood pressure (<120/80 mm Hg).<sup>4,11,12</sup>

An additional rationale for use of the term prehypertension rather than highnormal or normal blood pressure is that the new classification would be more likely to make the affected individual follow healthcare recommendations; the word ‘high’ is often ignored and ‘normal’ is overvalued.<sup>13</sup>

The JNC 7 leaned from the experience of writers of guidelines for other health problems, such as diabetes, cutaneous basal cell carcinoma and colonic adenomatous polyps. In each of these conditions, it was once popular to classify individuals as having ‘prediabetes’, ‘precancerous skin lesion’ and ‘pre-malignant polyps’, which presumably made the individual more likely to follow the recommendations made by their health care provider to avoid future disease outcomes.<sup>13</sup>

### **Against Prehypertension Terminology**

Arguments against using the term prehypertension for the blood pressure range 120–139/80–89 mm Hg include: the inhomogeneity of the prehypertension category because the risk of progressing to hypertension and developing

cardiovascular events is higher in patients with blood pressure 130–139/85–89 mm Hg range than in those with blood pressure 120–129/80–84 mm Hg and concern that the term prehypertension would create anxiety among the general public and would generate unnecessary medical visits.<sup>1,2</sup>

In the literature authors mention that from the prehypertensive range upward, the effect of blood pressure on cardiovascular risk is progressive and continuous. It is hard to understand what is ‘pre’ about it. The term is misleading as it implies that it is solely a precursor of hypertension, but the epidemiologic evidence of added risk shows that it is much more than that. On the basis of these considerations some authors suggested to eliminate prehypertension and replaced with stage 1 hypertension while bumping up the current stage 1 and 2 to 2 and 3.<sup>1,2</sup>

### **Prevalence**

The publication of JNC 7 led to the initiation of population based surveys to describe the prevalence of pre hypertension and increased awareness of the importance of the problem by doctors and health organizations. The third national Health and nutrition examination survey (NHANES III) 1999–2000 reported that the overall prevalence of prehypertension in the United States was 31%, higher in men than in women, and was higher in obese than in normal weight persons.<sup>14</sup> On the basis of the NHANES 2005–2006 data, an estimated 25% of the US population aged 20 years or older has prehypertension, including over 32 million men and 21 million women.<sup>15</sup>

**Table 1: Worldwide prevalence of prehypertension**

Study	Year	Prevalence	
		Men	Women
Framingham MA	1948	43.0	39.0
Framingham MA	1968-87	43.0	36.0
Israel	1991-99	50.6	35.9
NHANES USA	1999-2000	39.0	23.1
Keelung, Taiwan	1999-2003	40.2	30.9
NHANS, Korea	2001	41.9	25.9
Attica, Greece	2001-2002	43.0	35.0
Korea	2002	46.0	-
North India	2002	44.0	-
Chennai, India	2003	46.6	49.8
Porto, Portugal	2003-04	25.4	18.8

The prevalence of prehypertension in the US is 31%, while hypertension and normotension are 29% and 39% respectively. Thus, 60% of US adults have prehypertension or hypertension.<sup>6,16</sup> The age-adjusted prevalence of prehypertension was greater in men (39.0%) than in women (23.1%) and it was lower at older ages because of a higher prevalence of hypertension.<sup>16</sup> Of note, the prevalence of prehypertension was increased in all demographic groups in the National Health and Nutrition Examination Survey (NHANES) 1999-2000 as

compared with 1988-1994.<sup>14</sup> In the 2005 Korean NHANES data, the prevalence of prehypertension in adults aged 30 years or over was 29.1% (37.4% in men and 21.2% in women), and this was almost the same as the US data and they were also consistent with the recent estimates from around the globe.

### **Indian Scenario**

A study conducted to evaluate the predictors and correlates of prehypertension (PreHTN) among adults in Chennai, India found prehypertension in 46.6% of the men and 49.8% of the women. PreHTN was prevalent in 47.4% of adults, and another 34.7% had hypertension (Stage I, 20%, and Stage II, 14.7%). In urban India less than 18% of adults have normal BP of less than 120/80 mm Hg.<sup>7</sup>

### **Classification**

JNC7 introduced prehypertension in place of normal and high normal BP. Another change in classification from JNC 6 is the combining of stage 2 and stage 3 hypertension into a single stage 2 category. This revision reflects the fact that the approach to the management of the former two groups is similar.<sup>1,2</sup>

### **Reasons for creating a classification of prehypertension**

- Increase awareness of lifetime risk of hypertension
- Increase awareness of increased risk of cardiovascular complications
- Identify individuals in whom early intervention by lifestyle modifications could lower blood pressure
- Decrease the rate of progression to hypertension with age

- Prevent hypertension entirely

**Table 2. Blood pressure classification<sup>1,2</sup>**

<b>JNC 7</b>	<b>JNC 6</b>	<b>Systolic BP (mm Hg)</b>		<b>Diastolic BP (mm Hg)</b>
Normal	Optimal	< 120	and	< 80
Prehypertension		120 – 129	or	80 – 89
-	Normal	120 – 129	and	80- 84
-	High normal	130 – 139	or	85 – 89
<b>Hypertension</b>				
Stage 1	Stage 1	140 – 159	or	90 – 99
Stage 2		160	or	100
-	Stage 2	160 – 179	or	100 – 109
-	Stage 3	180	or	110

**Pathophysiology of hypertension and prehyperetension**

No single or specific cause is known for most cases of hypertension and prehypertension. The condition is referred to as primary in preference to essential. Since persistent hypertension can develop only in response to an increase in cardiac output or a rise in peripheral resistance, defects may be present in one or more of the multiple factors that affect these two forces as shown in the figure 1. The interplay of various derangements in factors affecting



women with prehypertension (mean blood pressure 130/78 mm Hg) were older (62.6 years versus 60.7 years), had a higher BMI (28.9 kg/m<sup>2</sup> versus 26.9 kg/m<sup>2</sup>), had a higher prevalence of diabetes mellitus (3.0% versus 1.8%) and a higher prevalence of high cholesterol (10.2% versus 8.3%). Together, these observations underscore the importance of global cardiovascular risk assessment in patients with prehypertension to optimize preventive and therapeutic strategies for these individuals.<sup>17</sup>

The risk ratios for obesity, dyslipidemia, insulin resistance, metabolic syndrome and diabetes are all greater in the prehypertensive subjects than those in the normotensive subjects and they are intermediate between those risk ratios for the subjects with normotension and hypertension.<sup>18-21</sup> Obesity is often associated with prehypertension.<sup>6,16,21,22</sup> Both general and abdominal obesity could be responsible for the risk of prehypertension.<sup>18</sup> In several studies, a higher body mass index (BMI) was the strongest predictor of prehypertension.<sup>19,22,23</sup> Prehypertensive individuals are more likely to have diabetes,<sup>21</sup> impaired fasting glucose,<sup>22</sup> metabolic syndrome,<sup>23</sup> hypercholesterolemia,<sup>16,23</sup> raised levels of low density lipoprotein cholesterol (LDL cholesterol) and triglycerides<sup>19,22</sup> and reduced levels of high density lipoprotein cholesterol (HDL cholesterol)<sup>19,22</sup> than normotensive individuals. Risk factors such as C-reactive protein, serum tumor necrosis factor, interleukin 6, and tumor necrosis factor-[alpha],<sup>24,25</sup> amyloid A, homocysteine,<sup>24</sup> resistin, adiponectin<sup>26</sup> and oxidative stress<sup>27</sup> are also more common in people with prehypertension than in those people with normal BP.

Data from epidemiological studies and clinical trials have demonstrated that elevations in resting heart rate and reduced heart-rate variability are

associated with higher cardiovascular risk. In the Framingham Heart Study, an average resting heart rate of 83 beats per minute was associated with a substantially higher risk of death from a cardiovascular event than the risk associated with lower heart rate levels.<sup>28</sup>

Moreover, reduced heart-rate variability was also associated with an increase in cardiovascular mortality.<sup>29</sup> No clinical trials have prospectively evaluated the impact of reduced heart rate on cardiovascular outcomes.

A study conducted to evaluate the predictors and correlates of prehypertension (PreHTN) among adults in Chennai, India identified risk factors that predict HTN were age, sex, smoking, alcohol intake, sedentary lifestyle, and type of work.<sup>16</sup>

### **Symptoms and Signs**

Prehypertension is almost always asymptomatic, so that patient may be unaware of the consequent progressive cardiovascular damage for as long as 10 to 20 years. Symptoms often attributed to hypertension headache, tinnitus, dizziness and fainting may be observed just as commonly in the pre and normotensive population.

Many symptoms attributable to the elevated BP are psychogenic in origin, often reflecting hyperventilation induced by anxiety over the diagnosis of a lifelong, insidious disease that threatens well being and survival.

## **Cardiovascular diseases and subsequent adverse events**

### ***Progression to hypertension***

Several studies have shown that individuals with prehypertension are at a greater risk for progression to hypertension than those individuals who are normotensive. The rate of progression of prehypertension to hypertension can be relatively rapid, and particularly for those individuals whose BPs lie in the upper prehypertensive range and for the elderly individuals. In the Framingham Heart Study, a stepwise increase in the incidence of hypertension occurred across the three non-hypertensive BP categories; 5.3% of the participants with optimum BP, 17.6% with normal, and 37.3% with high normal BP aged below 65 years progressed to hypertension over 4 years. Corresponding rates for patients 65 years and older were 16.0%, 25.5% and 49.5%, respectively.<sup>1,2</sup>

Obesity and weight gain also contributed to progression; a 5% weight gain on follow-up was associated with 20-30% increased odds for hypertension.<sup>11</sup> The data obtained from two British Health and Lifestyle Surveys conducted 7 years apart estimated that RR for the normal BP group was 2.0 and that for the high-normals was 2.9. In the TRial Of Preventing Hypertension (TROPHY) study, 40% of the prehypertensive individuals receiving a placebo developed hypertension over 2 years of follow-up. Because of these rates of progression, annual or biannual monitoring of BP in prehypertensive persons would seem appropriate.<sup>30</sup> A community-based integrated screening program in Keelung, Taiwan is the largest study of this type.<sup>31</sup> That study showed that prehypertension progresses or regresses and the adjusted progression rate for hypertension is age-

dependent and progression to stage 1 hypertension was positively related to the male gender, a higher waist circumference and having parents with hypertension. Data indicates the 3-year progression rate to hypertension among the prehypertensive local residents aged 45 or over is 56.4% (56.9% for the men and 55.9% for the women).<sup>32</sup>

### ***Cardiovascular***

The 1999 to 2000 NHANES data suggested that 64% of prehypertensive subjects have more than one CVD risk factor (94% for the persons 60 years or over). The people with prehypertension were 1.65 times more likely to have at least 1 other adverse risk factor than were those with normotension ( $p < .001$ ).<sup>16</sup>

Prehypertension also accelerates the development of left ventricular (lv) hypertrophy and diastolic dysfunction. The population based MONICA (Monitoring of Trends and Determinations in Cardiovascular Disease) – Augsburg/Kora (Cooperative research in the region of augsburg) study compared echocardiographic data from 119 individuals with prehypertension that persisted over the decade from 1994 or 1995 to 2004 or 2005 with data from 142 individuals in whom blood pressure remained normal over this time.<sup>33</sup> Over these 10 years, prehypertensive individuals had a significantly greater age related increase in lv wall thickness (11.9% versus 4.7%,  $P < 0.001$ ) and lv mass (15.7% versus 8.6%,  $P = 0.006$ ) and an increased incidence of lv concentric remodeling (hazard ratio [Hr] 10.7; 95% CI 2.82– 40.4) and lv hypertrophy (Hr 5.3; 95% CI 1.58–17.9), compared with individuals with normal blood pressure.<sup>34</sup>

The adjusted odds ratio for incident diastolic dysfunction was 2.52 (95% Ci 1.0–6.3) for the prehypertensive group. Thus, persistent prehypertension accelerates the development of lv hypertrophy and diastolic dysfunction.

### ***Cardiovascular morbidity and mortality***

Prehypertension has been associated with a variety of cardiovascular diseases and with increased cardiovascular associated and all cause mortality in a number of large cohort studies. In the Framingham Heart study, prehypertension, particularly the subclass previously referred to as high normal blood pressure (130–139/85–89 mm Hg), was associated with an increased incidence of cardiovascular disease, including myocardial infarction and coronary artery disease, but not stroke.<sup>12,35</sup> An analysis from WHI, which included 60,785 postmenopausal women, demonstrated that prehypertension was associated with an even wider spectrum of cardiovascular disease, including myocardial infarction, stroke, hospitalized heart failure, any cardiovascular event, and cardiovascular death.<sup>17</sup> 12 year follow up data from a cohort of participants in NHANES II also demonstrated an association between prehypertension and increased all cause and cardiovascular mortality.<sup>36</sup>

The increment in cardiovascular risk associated with progression from normotension to prehypertension is similar to that associated with the progression from prehypertension to hypertension. In the MONICA study, participants who transitioned from normotension to the upper levels of prehypertension had the same increase in risk of cardiovascular events (Hr 1.57; 95% CI 1.06– 2.33) as

those who progressed from the lower level of prehypertension to the hypertensive range (Hr 1.64; 95% Ci 1.19–2.26).<sup>33</sup>

These findings underscore both the importance of global cardiovascular risk assessment and the need for clinical trials to evaluate the efficacy of global cardiovascular risk reduction through primordial prevention in this large at risk population group.

### ***Incidence of cardiovascular disease, its risks and the subsequent events***

Prehypertension is associated with an increased incidence of CVD, and particularly in those individuals with upper range prehypertensive BP levels and those individuals with diabetes or glucose intolerance.<sup>21,37,38</sup> The Framingham Heart Study<sup>12</sup> investigated the association between the blood-pressure category at baseline and the incidence of CVD on follow-up among 6859 participants who were initially free of hypertension and CVD. The 10-year cumulative incidence of CVD in the subjects with high-normal BP was 4% for women and 8% for men who were 35 to 64 years old, respectively; for the older subjects (65 to 90 years old), the incidence was 18% for women and 25% for men. As compared with optimal BP, high-normal BP was associated with a riskfactor- adjusted hazard ratio for CVD of 2.5 for women and 1.6 for men. The same conclusion was reached in a meta-analysis of 61 prospective observational studies.<sup>5</sup>

The NHANES I Epidemiologic Follow-Up Study (NHEFS) and the NHANES II Mortality Study (1992) have also concluded that prehypertension significantly increases the risk for cardiovascular events.<sup>14</sup> In the Strong Heart Study<sup>21</sup> there was a synergistic effect of prehypertension and diabetes on the

occurrence of CVD events; the hazard ratios for CVD were 3.70 for those individuals with both prehypertension and diabetes, 1.80 for those individuals with prehypertension alone and 2.90 for those individuals with diabetes alone. Impaired glucose tolerance or impaired fasting glucose also greatly increased the CVD risk in prehypertensive people.

## **Complications**

### ***Target organ damage***

Prehypertension is associated with subclinical cardiovascular disease, including both microvascular and macrovascular pathology. People with prehypertension also have greater degrees of target-organ damage than do the normotensive individuals.

### ***Retinopathy***

Generalized retinal arteriolar narrowing is an important sign of systemic hypertension, and a lower arteriolar:venular diameter ratio can predict risk of hypertension.<sup>39,40</sup> Accordingly, the Rotterdam study, a prospective, population based study with 1,900 participants ( 55 years of age, including 739 with normal blood pressure and 1,161 with prehypertension), found that individuals with prehypertension had significantly smaller arteriolar and venular diameters and arteriolar venular ratios than normotensive individuals, indicating the presence of microvascular damage.<sup>41</sup>

### ***Microalbuminuria***

Microalbuminuria an organ specific manifestation of generalized endothelial dysfunction that is associated with increased risk of cardiovascular disease is more common in individuals with prehypertension than in those with normal blood pressure.<sup>42-44</sup> The appearance of albumin in the urine is a direct result of increased glomerular capillary permeability and serves as a marker for increased vascular permeability to proteins from other organs (for example, large arteries, heart and brain).<sup>45</sup>

Factors that confer a predisposition to microalbuminuria, such as inflammation, oxidative stress and increased blood pressure, also have a role in the pathogenesis of microvascular and macrovascular disease, thus, treatments that reduce microalbuminuria lower the risk of cardiovascular events.

Individuals with prehypertension often have subclinical atherosclerosis, manifested by increased common carotid artery intima media thickness<sup>46</sup> and increased calcium deposition in the coronary arteries.<sup>47</sup> Serial observations, carried out as part of the Coronary Artery Risk Development in Young Adults (CARDIA) study, demonstrated that prehypertension, especially systolic prehypertension, before the age of 35 was significantly associated with coronary calcium in later life, even after adjusting for elevations in blood pressure after 35 years of age, other coronary risk factors and participant characteristics.<sup>47</sup>

## **Management**

### **Patient evaluation**

Evaluation of hypertensive patients has three objectives: (1) to assess lifestyle and identify other cardiovascular risk factors or concomitant disorders that may affect prognosis and guide treatment ; (2) to reveal identifiable causes of high BP; and (3) to assess the presence or absence of target organ damage and CVD.<sup>1,2</sup>

Patient evaluation is made through medical history, physical examination, routine laboratory tests, and other diagnostic procedures. The physical examination should include: an appropriate measurement of BP, with verification in the contralateral arm; accurate heart rate measurement, an examination of the optic fundi; a calculation of body mass index (BMI) (measurement of waist circumference is also very useful); an auscultation for carotid, abdominal, and femoral bruits; a palpation of the thyroid gland; a thorough examination of the heart and lungs; an examination of the abdomen for enlarged kidneys, masses, distended urinary bladder, and abnormal aortic pulsation; a palpation of the lower extremities for edema and pulses; and neurological assessment.<sup>1,2</sup>

### **Laboratory tests**

Routine laboratory tests recommended include a 12-lead electrocardiogram; urinalysis; blood glucose and hematocrit; serum potassium, creatinine (or the corresponding estimated glomerular filtration rate [eGFR]) and a lipid profile (after a 9 to 12 hour fast) that includes high-density lipoprotein

cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides.<sup>1,2</sup>

Optional tests include measurement of urinary albumin excretion or albumin/creatinine ratio (ACR) except for those with diabetes or kidney disease where annual measurements should be made. The presence of albuminuria, including microalbuminuria, even in the setting of normal GFR, is also associated with an increase in cardiovascular risk.<sup>1,2</sup>

Additionally, three emerging risk factors (1) high-sensitivity C-reactive protein (HS-CRP); a marker of inflammation; (2) homocysteine; and (3) elevated heart rate may be considered in some individuals, particularly those with CVD but without other risk-factor abnormalities.<sup>48</sup>

Treadmill test has been used to evaluate CAD probability and other factors like autonomic dysfunction, sympathetic overactivity.

### ***TMT testing***

Exercise testing is a noninvasive tool to evaluate the cardiovascular system's response to exercise under carefully controlled conditions. Exercise is the body's most common physiologic stress, and it places major demands on the cardiopulmonary system. Thus, exercise can be considered the most practical test of cardiac perfusion and function. The exercise test, alone and in combination with other noninvasive modalities, remains an important testing method because of its high yield of diagnostic, prognostic, and functional information. The test is mainly used to estimate prognosis and to determine functional capacity, the

likelihood and extent of coronary artery disease (CAD), and the effects of therapy. Exercise testing has a sensitivity of 78% and a specificity of 70% for detecting coronary artery disease.<sup>48</sup>

#### Diagnostic indications for exercise testing

- Assessment of chest pain in patients with intermediate probability for coronary artery disease
- Arrhythmia provocation
- Assessment of symptoms (for example, presyncope) occurring during or after exercise.<sup>48</sup>

#### Protocol

Though various protocols like Naughton and ramp protocol are in vogue, the popular one is Bruce protocol. There is also a Modified Bruce Protocol for those with lower functional capacity or for early post infarction evaluation. Standard Bruce Protocol has seven three minute stages. In stage I, the gradient is 10% and it rises 2% per stage. The starting speed is 1.7 MPH and increased in increments of 0.8 to 0.9 MPH per stage. In Modified Bruce Protocol Stage I has a gradient of zero and stage II a gradient of five percent, speed is the same in the first three stages of Modified Bruce Protocol (1.7 MPH). Stage 3 of Modified Bruce Protocol is equivalent to stage I of Standard Bruce Protocol. Further stages are similar to Bruce Protocol though the number of the stage will be higher by a magnitude of 2.<sup>48</sup>

Contraindications for exercise testing

- Acute myocardial infarction (within 4-6 days)
- Unstable angina (rest pain in previous 48 hours)
- Uncontrolled heart failure
- Acute myocarditis or pericarditis
- Acute systemic infection
- Deep vein thrombosis
- Uncontrolled hypertension (systolic blood pressure >220 mm Hg, diastolic >120 mm Hg)
- Severe aortic stenosis
- Severe hypertrophic obstructive cardiomyopathy
- Untreated life threatening arrhythmia
- Dissecting aneurysm
- Recent aortic surgery

Reasons for stopping a test

*Electrocardiographic criteria*

- Severe ST segment depression (>3 mm)
- ST segment elevation >1 mm in non-Q wave lead
- Frequent ventricular extrasystoles (unless the test is to assessment ventricular arrhythmia)
- Onset of ventricular tachycardia
- New atrial fibrillation or supraventricular tachycardia

- Development of new bundle branch block (if the test is primarily to detect underlying coronary disease)
- New second or third degree heart block
- Cardiac arrest

#### *Symptoms and signs*

- Patient requests stopping because of severe fatigue
- Severe chest pain, dyspnoea, or dizziness
- Fall in systolic blood pressure (>20 mm Hg)
- Rise in blood pressure (systolic >300 mm Hg, diastolic >130 mm Hg)
- Ataxia

#### Diagnosis

Any abnormal electrocardiographic changes must be interpreted in the light of the probability of coronary artery disease and physiological response to exercise. A normal test result or a result that indicates a low probability of coronary artery disease is one in which 85% of the maximum predicted heart rate is achieved with a physiological response in blood pressure and no associated ST segment depression.

#### Findings suggesting high probability of coronary artery disease

- Horizontal ST segment depression of 2 mm.
- Downsloping ST segment depression.
- Early positive response within six minutes.
- Persistence of ST depression for more than six minutes in recovery.

- ST segment depression in five or more leads.
- Exertional hypotension.

A test that indicates a high probability of coronary artery disease is one in which there is substantial ST depression at low work rate associated with typical angina-like pain and a drop in blood pressure. Deeper and more widespread ST depression generally indicates more severe or extensive disease.<sup>48</sup>

### Limitations

The specificity of ST segment depression as the main indicator of myocardial ischaemia is limited. ST segment depression has been estimated to occur in up to 20% of normal individuals on ambulatory electrocardiographic monitoring. There are many causes of ST segment changes apart from coronary artery disease, which confound the result of exercise testing.

### **Treatment**

The primary reasons to consider treating prehypertension are the substantial progression to hypertension and the association with increased CVD. Many studies have shown the progression to hypertension. The current stage of prehypertension includes a broad range of blood pressure. This presents a challenge in defining a treatment paradigm for these individuals because the progression rates vary widely.

Based on the Framingham and the TROPHY studies,<sup>11,30</sup> the four year progression rate for those individuals with high-normal BP is approximately 40% (37.3-49.5%). This 4-year rate varies by age and the baseline BP level. Therefore,

upper range prehypertensive patients (130-139/85-89 mm Hg) have a high rate of progression over 4 years (40-63%), which may warrant a more aggressive approach than for those individuals in the lower range (120-129/80-84 mm Hg).

The Strong Heart Study,<sup>21</sup> the ARIC Study<sup>38</sup> and the Framingham Heart Study<sup>12</sup> have shown that prehypertension is itself associated with higher cardiovascular risk. How best to manage prehypertension has been the subject of recent debate. At present, the JNC-7 report recommends that adoption of healthy lifestyles by all individuals is critical for the prevention of high BP and to decrease the BP and cardiovascular risk. Drug therapy is recommended for prehypertensives with diabetes or chronic kidney disease.

### ***Drug therapies***

All the hypertension guidelines now recommend drug therapy for the patients with diabetes and chronic kidney disease and who are in the prehypertensive range.<sup>1,2,49-51</sup> Others advocate a lower-than-usual BP goal for people with established cardiovascular disease or those at high risk (e.g. African Americans).

The TROPHY study is the first randomized, placebo controlled, double-blinded clinical trial of pharmacologic intervention for treating prehypertension.<sup>30</sup> It was designed to study whether 2 years of treatment with the angiotensin receptor blocker (ARB) candesartan cilexetil at 16 mg daily prevents or delays the development of hypertension during treatment and for up to 2 years after discontinuing treatment in those subjects who are in the upper half of the JNC-7 stage of prehypertension (systolic blood pressure 130-139 mm Hg or diastolic

blood pressure 85-89 mm Hg). 809 study participants were there in total. The primary outcome of the trial was the development of hypertension or the development of target organ damage or diabetes. The results demonstrated that pharmacologic treatment can prevent or postpone the development of hypertension with a 66.3% reduction in the incidence of hypertension relative to placebo over the first 2 years (26.8% absolute reduction). Over all four years, including drug withdrawal of 2 years, there was a 15.6% reduction in the incidence of hypertension relative to placebo (9.8% absolute reduction).

In addition, treatment with 16 mg of candesartan cilexetil was not only safe but also well tolerated with a low report of side-effects which was not significantly different from the placebo group. Yet to translate the results of the TROPHY study into daily practice is another challenge because of the current high cost of the required medication, and candesartan did not significantly reduce cardiovascular disease events. Other drug therapy trials like the Program to Improve Life and Longevity (PILL) and the Aliskiren in Visceral Obesity at Risk Patients Out-comes Research (AVIATOR) are now ongoing. On-going research will probably identify which individuals with blood pressure in the prehypertensive range would benefit from drug treatment.

Further study is needed to determine whether pharmacological treatment of blood pressure in prehypertension provides a costeffective strategy for preventing cardiovascular disease outcomes.

Additional questions concern appropriate choices and doses of agents and duration of treatment. Arguments in favor of the use of anti hypertensive drugs

for prehypertension are that the drugs are more convenient and more likely to be adhered to than complex lifestyle modifying regimens and that the drugs are already accepted for use in certain high risk individuals with prehypertension (that is, in those with blood pressure  $\geq 130/80$  mm Hg and with diabetes mellitus, chronic kidney disease or coronary artery disease).

In the absence of further information about these issues and in light of the fact that lifestyle approaches favorably influence global cardiovascular risk as well as blood pressure, lifestyle modification is currently the first choice for the treatment of individuals with prehypertension who do not have comorbid conditions that would mandate blood pressure reduction by use of pharmacological agents. Assessment of global cardiovascular risk should be used to guide the decision of whether to use antihypertensive agents in patients with prehypertension.<sup>40</sup>

### ***Lifestyle modifications***

Lifestyle modifications are currently recommended to lower BP in those individuals with prehypertension or those individuals who are at risk for hypertension.<sup>1,2,49-51</sup> Major lifestyle modifications include;

- Weight reduction in those individuals who are overweight or obese.
- Adoption of the Dietary Approaches to Stop Hypertension eating plan (DASH) dietary sodium reduction.<sup>7,52,53</sup>
- Physical activity.
- Moderation of alcohol consumption.

Nonpharmacological therapies have not prevented cardiovascular events in long-term clinical trials, but lifestyle modifications are necessary for the treatment and prevention of diabetes, dyslipidemia, obesity and other CVDs associated with prehypertension. Weight loss is likely to be the most effective lifestyle modification because of the high prevalence of being overweight and obese. In the Framingham study, the participants who successfully reduced their weight by 6.8 kg or more over a 4-year period decreased their risk of developing hypertension by 21-29%. In the Keelung study, the strongest age-independent predictor of regression from prehypertension to normotension was reduction of the BMI.<sup>31</sup>

### **Prevention**

To prevent BP levels from rising, primary prevention measures should be introduced to reduce or minimize these causal factors in the population, particularly in individuals with prehypertension.

A population approach that decreases the BP level in the general population by even modest amounts has the potential to substantially reduce morbidity and mortality or at least delay the onset of hypertension. For example, it has been estimated that a 5 mm Hg reduction of SBP in the population would result in a 14 percent overall reduction in mortality due to stroke, a 9 percent reduction in mortality due to CHD, and a 7 percent decrease in all-cause mortality.<sup>5</sup>

Barriers to prevention include cultural norms; insufficient attention to health education by health care practitioners; lack of reimbursement for health

education services; lack of access to places to engage in physical activity; larger servings of food in restaurants; lack of availability of healthy food choices in many schools, worksites, and restaurants; lack of exercise programs in schools; large amounts of sodium added to foods by the food industry and restaurants; and the higher cost of food products that are lower in sodium and calories.<sup>54</sup> Overcoming the barriers will require a multipronged approach directed not only to high-risk populations, but also to communities, schools, worksites, and the food industry.

The recent recommendations by the American Public Health Association and the NHBPEP Coordinating Committee that the food industry, including manufacturers and restaurants, reduce sodium in the food supply by 50 percent over the next decade is the type of approach which, if implemented, would reduce BP in the population.<sup>56,55</sup>

To conclude Prehypertension is highly prevalent and is associated with the traditional cardiovascular risk factors linked to hypertension, such as obesity, diabetes mellitus and dyslipidemia. Patients with prehypertension have an increased risk of cardiovascular morbidity and mortality compared with patients who have normal blood pressure (<120/80 mm Hg). Lifestyle modifications with pharmacological therapy are recommended for all patients with prehypertension and effectively reduce cardiovascular risk. Outcome studies are needed to establish the value of pharmacologic therapy for the treatment of prehypertension.

## **METHODOLOGY**

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with prehypertension during the period of January 2009 to December 2009.

### **Study design**

The study design was one year cross sectional study.

### **Study period and duration**

The present one year study was conducted during the period of January 2009 to December 2009.

### **Method of collection of data**

### **Source of Data**

Prehypertensives attending outpatient department and/or in patient department reporting Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during study period were chosen by simple random method using random number table.

### **Sample size**

Hundred (100) patients with prehypertension were selected for the study.

### **Sampling procedure**

The sample size was calculated based on the formula as mentioned below.

$$n = 4 \times p \times q / d^2$$

$$n = 4 \times 50 \times 50 / 10^2$$

$$n = 100$$

Where  $p$  = prevalence i.e. 50%

$$q = 100 - p$$

$d$  = Standard error (10)

### **Selection criteria**

#### ***Inclusion Criteria***

- Patients diagnosed to have prehypertension
  - Systolic blood pressure – 120 to 139 mm Hg.
  - Diastolic blood pressure – 80 to 89 mm Hg.
- Age more than 18 years.

#### ***Exclusion Criteria***

- Known case of hypertension (SBP more than 140 mm Hg, DBP more than 90 mm Hg).
- Normal individuals having SBP less than 120 mm Hg and DBP less than 80 mm Hg.

## Procedure

Patients attending to Department of Medicine or admitted in the wards of Medicine Department at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, were evaluated based on selection criteria. Three BP readings, five minutes apart were taken and mean of second and third reading was selected as final blood pressure. The patients were selected by detailed medical history and physical examination. The study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belgaum. The selected patients were briefed about the nature of the study, the interventions used and a written informed consent was obtained (Annexure-I).

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded. Body mass index was calculated based on formula;

$$\text{Body Mass Index} = \frac{\text{Weight (Kg)}}{\text{Height}^2 \text{ (m)}}$$

Body mass index in the range of less than 18.5 kg/m<sup>2</sup> were considered as underweight, 18.5 to 24.9 kg/m<sup>2</sup> were considered as normal, 25.0 to 29.9 kg/m<sup>2</sup> were considered as overweight and more than 30 kg/m<sup>2</sup> were considered as obese.<sup>19,22,23</sup>

The WHR was calculated as;

$$\text{WHR} = \frac{\text{Waist circumference (Cms)}}{\text{Maximum hip circumference (Cms)}}$$

Waist hip ratio of less than 0.9 in males and 0.85 in females was considered as normal.<sup>19</sup>

Routine investigations such as blood group, haemogram (haemoglobin, total count, differential count, erythrocyte sedimentation rate), urine routine and microscopy were done.

Others tests like fasting blood sugar, post prandial blood sugar, electrocardiogram were carried out.

Special tests such as renal functional tests (serum creatinine), Lipid Profile, Tread Mill Test and funduscopy were conducted and recorded.

### **Tread Mill Test**

All patients were subjected to TMT using Modified Bruce Protocol and interpretation were recorded including electrocardiograms, heart rate and blood pressure changes during rest, three stages of Modified Bruce Protocol and recovery period.

Hypertensive BP response was defined as maximum systolic BP more than 210 mm of Hg in males and 190 mm Hg in females.

Heart rate recovery time was termed blunted when heart rate failed to drop less than 18 beats in one minute after stopping of exercise.

Angiographic coronary artery disease (CAD) was calculated based on simple exercise test score which included clinical and TMT parameters (Table 3 and 4).

Treadmill test was said to be positive for inducible ischaemia in presence of;

- Horizontal ST segment depression of 2 mm.
- Downsloping ST segment depression.
- Early positive response within six minutes.
- Persistence of ST depression for more than six minutes in recovery.
- ST segment depression in five or more leads.
- Exertional hypotension.

**Table 3. Simple exercise test score for men**

Variable	Circle response	Sum	
Maximal heart rate	< 100 bpm = 30		<b>&lt; 40 = Low probability</b>
	100 to 129 bpm = 24		
	130 to 159 bpm = 18		
	160 to 189 bpm = 12		
	190 to 220 bpm = 6		
Exercise ST depression	1 – 2 mm = 15		<b>40 – 60 Intermediate Probability</b>
	> 2 mm = 25		
Age	> 55 Years = 20		
	40 to 55 years = 12		
Angina History	Definite typical = 5		
	Probable atypical = 3		
	Non cardiac pain = 1		
Hypercholesteromia ?	Yes = 5		
Diabetes	Yes = 5		
Exercise test induced angina	Occurred = 3		
	Reason for stopping = 5		
	Total score		

**Table 4. Simple exercise test score for women**

Variable	Circle response	Sum	
Maximal heart rate	< 100 bpm = 20		<b>&lt; 37 = Low probability</b>
	100 to 129 bpm = 16		
	130 to 159 bpm = 12		
	160 to 189 bpm = 8		
	190 to 220 bpm = 4		
Exercise ST depression	1 – 2 mm = 6		<b>37 – 57 Intermediate Probability</b>
	> 2 mm = 10		
Age	> 55 Years = 25		
	40 to 55 years = 15		
Angina History	Definite typical = 10		
	Probable atypical = 6		
	Non cardiac pain = 2		
Hypercholesteromia?	Yes = 10		
Diabetes	Yes = 10		
Exercise test induced angina ?	Occurred = 9		
	Reason for stopping = 15		
Estrogen status	Positive = - 5, Negative = + 5		
	Total score		

The change in various stages of TMT for SBP and DBP were calculated as below;

- **Delta 1:** Stage 1 BP – Resting BP
- **Delta 2:** Stage 2 BP – Stage 1 BP
- **Delta 3:** Stage 3 BP – Stage 2 BP

Some studies define hypertensive BP response as any stage delta SBP more than 55 mm Hg but in this study a delta parameters of more than 30 mm Hg was considered as a new level and these individuals were compared with other prehypertensives having delta less than 30 mm Hg.

### **Statistical analysis**

The results were tabulated and the data was analysed using rates, ratios and percentages of different clinical manifestations. The data was compared using chi-square test, ‘Z’ test and student ‘t’ test. A ‘p’ value of less than 0.05 was considered as statistically significant.

## RESULTS

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on Hundred (100) patients with prehypertension during the period of January 2009 to December 2009. The data obtained was tabulated and the analysis was done as below.

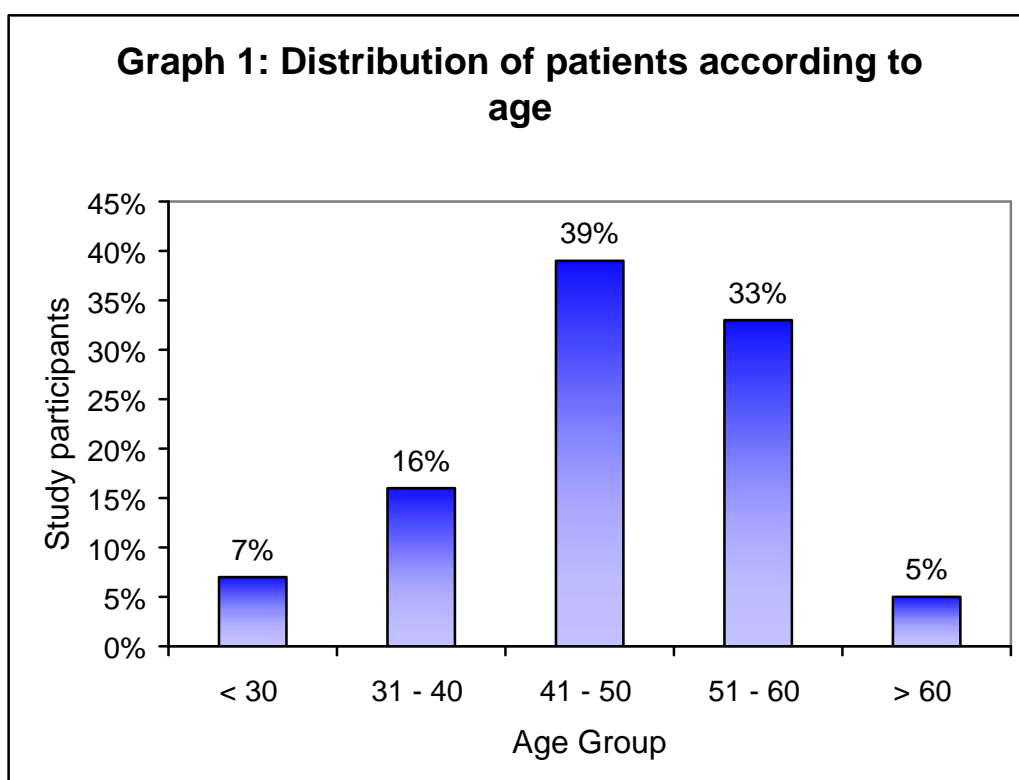
**Table 5. Distribution of patients according to gender**

Gender	Patients	
	Number	Percentage
Male	83	83
Female	17	17
<b>Total</b>	<b>100</b>	<b>100</b>

In the present study out of total 100 prehypertensives, majority were males (83%) and 17% were females.

**Table 6. Distribution of patients according to age**

Age (Years)	Patients	
	Number	Percentage
30	7	7
31 – 40	16	16
41 – 50	39	39
51 – 60	33	33
More than 60	5	5
<b>Total</b>	<b>100</b>	<b>100</b>



In the present study majority (39%) had age between 41 to 50 years followed by 51 to 60 years (33%), 31 to 40 years (16%), less than 30 years (7%)

and more than 60 years (5%). Overall the mean age of prehypertensives was  $46.82 \pm 9.73$  years.

**Table 7. Distribution of patients according to history**

History	Patients	
	Number	Percentage
Diabetes mellitus	26	26
Ischaemic heart disease	9	9
Diabetes mellitus with Ischaemic heart disease	4	4

In this study 26% of patients were known case of diabetes or history (clinical features) was suggestive of diabetes mellitus. Similarly history of Ischaemic heart disease was present in 9% subjects.

**Table 8. Distribution of patients according to family history**

Family History	Patients	
	Number	Percentage
Diabetes mellitus	35	35
Hypertension	34	34

The family history of diabetes and hypertension was present in 35% and 34% respectively.

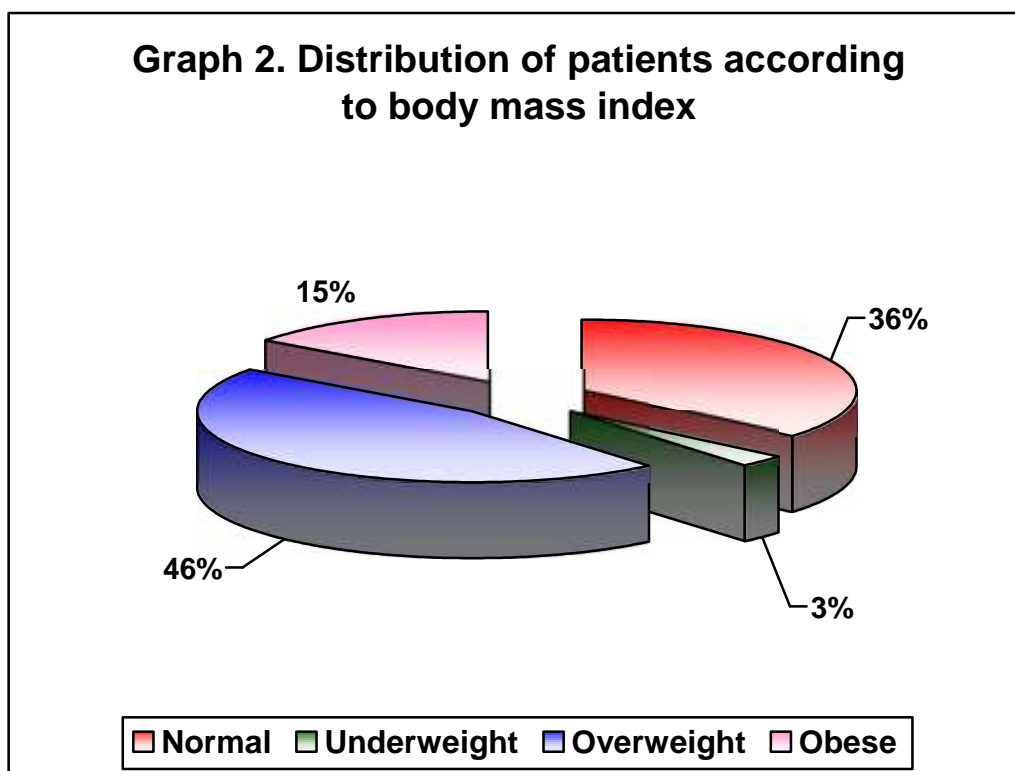
**Table 9. Distribution of patients according to habits**

Habits	Patients	
	Number	Percentage
Smoking	25	25
Alcohol	21	21
Smoking with Alcohol	12	12

25% of prehypertensives in present study were smokers and 21% were alcoholics with 12% being both alcoholics and smokers.

**Table 10. Distribution of patients according to body mass index**

Body Mass Index	Patients	
	Number	Percentage
Underweight (< 18.5 kg/m <sup>2</sup> )	3	3
Normal weight (18.5 to 24.9 kg/m <sup>2</sup> )	36	36
Overweight (25.0 to 29.9 kg/m <sup>2</sup> )	46	46
Obese (> 30 kg/m <sup>2</sup> )	15	15
<b>Total</b>	<b>100</b>	<b>100</b>



In the present study 61% patients were overweight (46%) or obese (15%); outnumbering the normal weight persons (36%) and underweight (3%). The mean weight of study participants was  $70.87 \pm 12.73$  Kg and mean BMI was  $25.91 \pm 3.95$  Kg/m<sup>2</sup>.

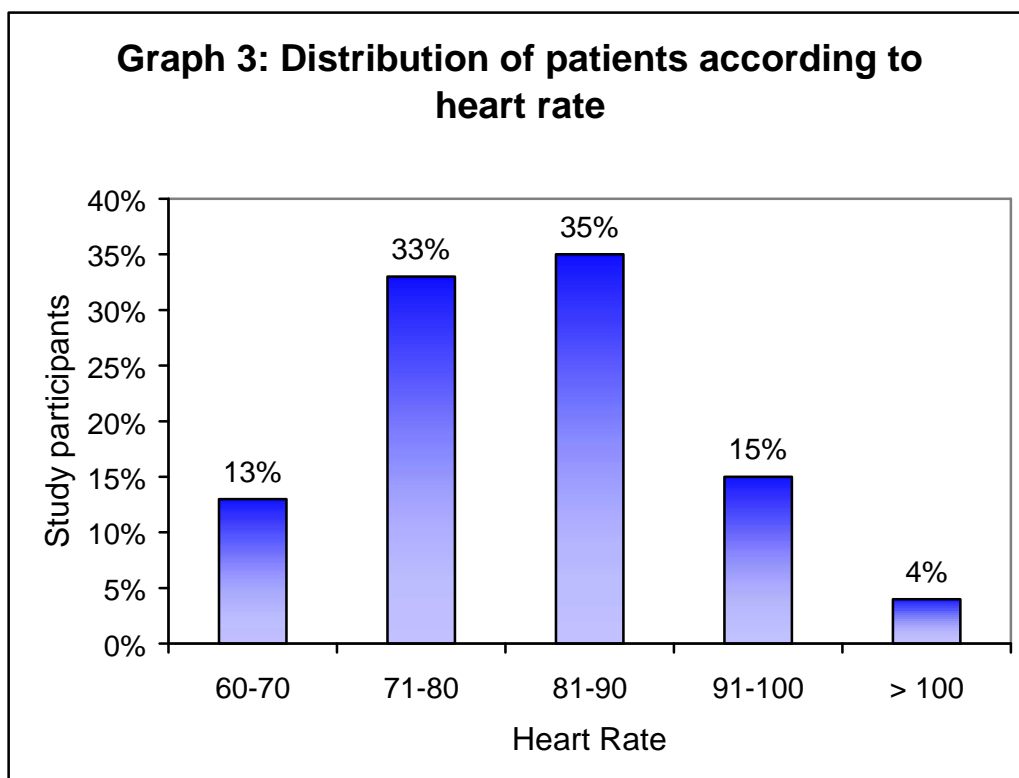
**Table 11. Distribution of patients according to Waist Hip Ratio**

Waist hip ratio	Patients	
	Number	Percentage
Normal	79	79
Abnormal	21	21
<b>Total</b>	<b>100</b>	<b>100</b>

The mean waist hip ratio of study participants was  $0.85 \pm 0.06$ . Majority (79%) of the patients were within the normal range and 21% were obese.

**Table 12. Distribution of patients according to heart rate**

Heart rate (/Min)	Patients	
	Number	Percentage
60 – 70	13	13
71 – 80	33	33
81 – 90	35	35
91 – 100	15	15
>100	4	4
<b>Total</b>	<b>100</b>	<b>100</b>



Mean basal heart rate of all prehypertensives was  $82.50 \pm 10.37$  beats/min. In the present study, 54% of patients had basal heart rate of more than 80 beats/min. (81 to 90 beats/min; 35%), (91 to 100 beats/min; 15%), (>100 beats/min; 4%) and 46% patients had heart rate in the normal range of 60 to 80 beats/min (60 to 70; 13%, 71 to 80; 33%). Even 4% individuals had their basal heart rate more than 100 beats/min.

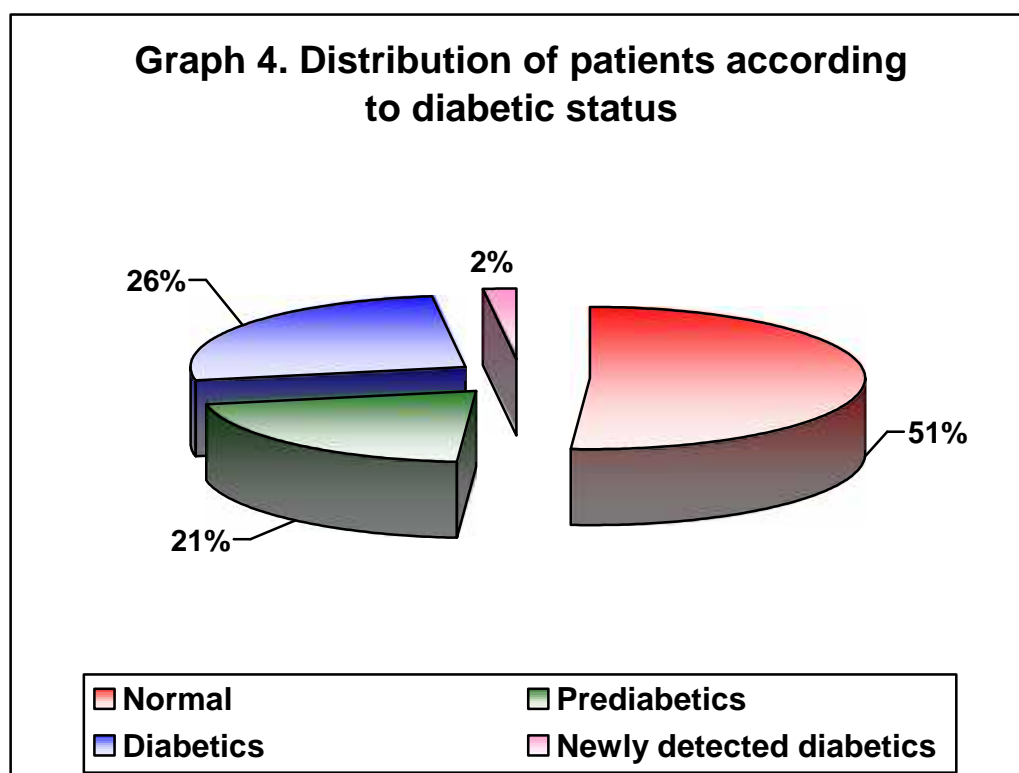
**Table 13. Distribution of patients according to blood pressure**

<b>Blood pressure (mm Hg)</b>	<b>Patients</b>	
	<b>Number</b>	<b>Percentage</b>
<b>SBP</b>		
120 – 129	49	49
130 – 139	51	51
<b>DBP</b>		
80 – 84	64	64
85 – 89	36	36
<b>Total</b>		

In the present study, 49% patients had their SBP in the range of 120-129 mm Hg, 51% had SBP from 130-139 mm Hg. Similarly DBP was 80-84 mm Hg in 64% and 85-89 mm Hg in 36% individuals.

**Table 14. Distribution of patients according to diabetic status**

Diabetic Status	Patients	
	Number	Percentage
Known cases of diabetics	26	26
Newly detected diabetics	2	2
Prediabetics	21	21
Normal	51	51
<b>Total</b>	<b>100</b>	<b>100</b>



In the present study, there were 28% diabetics and of them 2% were newly detected. Surprisingly, 21% were prediabetic based on ADA guidelines and 51% persons had their sugar levels in normal range.

**Table 15. Distribution of patients according to glomerular filtration rate**

<b>GFR (Creatinine clearance)</b>	<b>Patients</b>	
	<b>Number</b>	<b>Percentage</b>
Normal (>90 ml/min)	83	83
Deranged (<90 ml/min)	17	17

The present study showed deranged GFR less than 90 ml/min in 17% of subjects out of them 9% were diabetics and 2% were prediabetics and remaining (6%) were non diabetic prehypertensives. The mean GFR of study population was calculated as  $118.69 \pm 28.36$  ml/min.

**Table 16. Distribution of patients according to Lipid profile**

Lipid profile	Patients	
	Number	Percentage
<b>Serum Cholesterol</b>		
Desirable (<200)	66	66
Borderline high (200 – 239)	23	23
High (>240)	11	11
<b>LDL</b>		
Optimal (<130)	69	69
Borderline High (130 – 159)	22	22
High (>160)	9	9
<b>HDL</b>		
Low (<40)	54	54
High (>60)	7	7
<b>TG</b>		
Normal	63	63
Hypertriglyceredemia (>150)	37	37

In lipid profile according to ATEP III guidelines serum cholesterol was in desirable limits (less than 200) among 66% patients and borderline high (200 to 239) in 23% and high (more than 240) in 11% patients. The mean serum cholesterol levels among study participants was  $191.85 \pm 40.32$  mg/dL. Similarly LDL-C was optimal (less than 130) in 69%, borderline high (130 to 159) in 22% and high (more than 160) in 9% cases. The mean LDL levels among study participants was  $115.63 \pm 39.15$  mg/dL.

HDL was low in majority of patients (less than 40) in 54% patients and high in (7%) with 39% having normal HDL. The mean HDL levels among prehypertensives was  $45.61 \pm 19.38$  mg/dL.

The mean TG levels among study population was  $156.70 \pm 111.25$  mg/dL. Hypertriglyceridemia (TG more than 150) was seen in 37% of subjects.

**Table 17. TMT findings**

	<b>Patients</b>	
	<b>Number</b>	<b>Percentage</b>
<b>Angiographic CAD Probability</b>		
Low	39	39
Intermediate	46	46
High	15	15
<b>Heart rate recovery time</b>		
Normal	95	95
Blunted	5	5
<b>Inducible ischaemia</b>		
Positive	13	13
Negative	87	87
<b>Hypertensive BP response</b>		
Positive	16	16
Negative	84	84

Angiographic coronary artery disease probability calculated by simple exercise test score (Table 3 and 4) showed majority (61%) having; intermediate

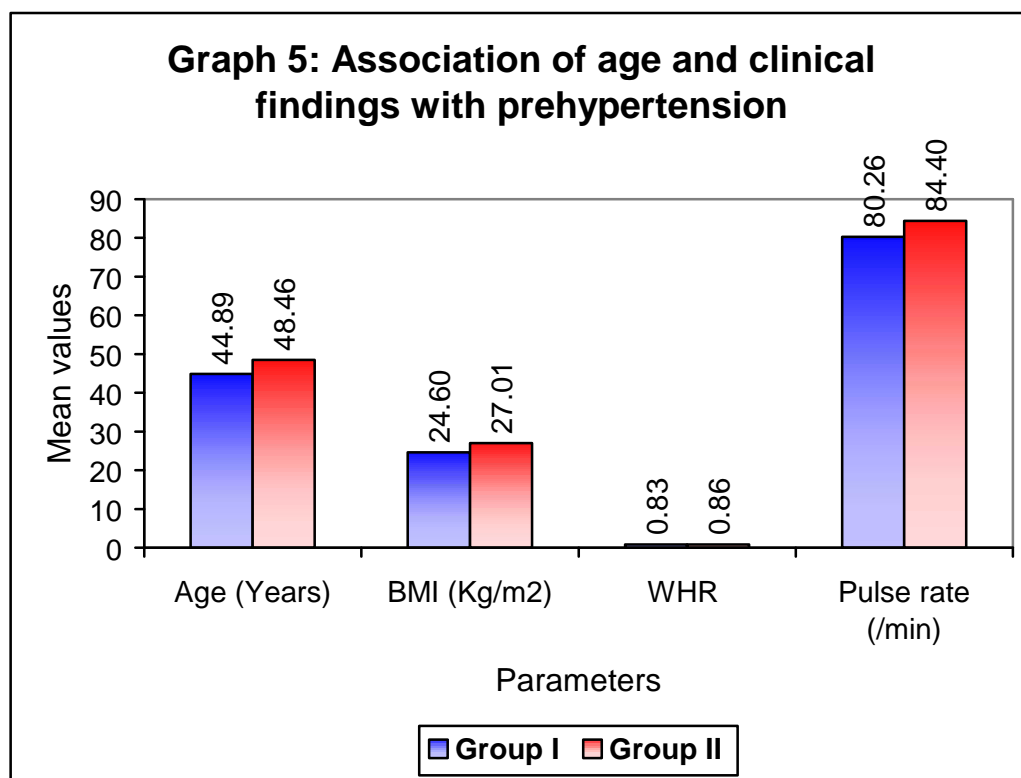
(46%) and high (15%) probability and (39%) subjects had low probability for angiographic CAD. TMT showed positive for inducible ischaemia in 13% subjects. Hypertensive BP response (SBP >210 mm Hg in males and >190 mm Hg in females) was seen in 16% subjects. Heart rate recovery time blunted which is marker of autonomic dysfunction was seen in 5% of prehypertensives. Average percentage fall in heart rate in those with normal heart rate recovery response was 30.23% in one minute of recovery as compared to 14.26% in those with blunted heart rate recovery time.

**Table 18. Association of age, clinical findings and laboratory profile with prehypertension**

Variables	Group I*(n=46)		Group II**(n=54)		t	DF	p value
	Mean	SD	Mean	SD			
Age	44.89	9.87	48.46	9.39	1.851	98	0.067
BMI	24.6	3.84	27.01	3.71	4.639	98	<0.001
WHR	0.83	0.05	0.86	0.04	3.332	98	0.001
Basal HR	80.26	9.87	84.4	10.48	2.022	98	0.046
<b>Laboratory profile</b>							
GFR	121	26.56	116.72	29.92	0.751	98	0.455
Cholesterol	178.73	34.23	203.01	42.00	3.133	98	0.002
LDL	106.93	35.03	123.03	41.21	2.084	98	0.040
HDL	46.32	20.03	45	18.96	0.338	98	0.736
TG	131.28	64.24	178.35	136.29	2.260	98	0.027

\* Blood pressure 120 to 129 / 80 to 84 mm Hg

\*\* Blood pressure 130 to 139 / 85 to 89 mm Hg



In the present study two groups were formed on basis of BP that is, Group I with SBP 120 to 129 mm Hg and DBP 80 to 84 mm Hg and Group II with SBP 130 to 139 mm Hg and DBP 85 to 89 mm Hg. Total number of persons in Group I and II were 46 and 54 respectively.

Subjects in group II previously called high normal (130-139 / 85-89 mm Hg) were older (mean age  $48.46 \pm 9.39$  years) than group I (120-139 / 80-84 mm Hg) but this was statistically not significant ( $p=0.067$ ).

Body Mass Index measure of obesity was more, ( $27.01 \pm 3.71$  kg/m<sup>2</sup>) in Group II as compared to Group I ( $24.60 \pm 3.84$  Kg/m<sup>2</sup>) with high statistical significance ( $p<0.001$ ) indicating that obesity is risk factor of prehypertension and hypertension and proposing that increase in obesity is associated with increase in blood pressure.

Waist hip ratio was significantly more ( $0.86 \pm 0.04$ ) in Group II compared to Group I ( $0.83 \pm 0.05$ ) ( $p=0.001$ ).

Patients in Group I had lower basal heart rate ( $80.2 \pm 9.8$  beats/min) compared to Group II with HR of ( $84.4 \pm 10.4$  beats/min) suggesting common etiology sympathetic overactivity or parasympathetic underactivity.

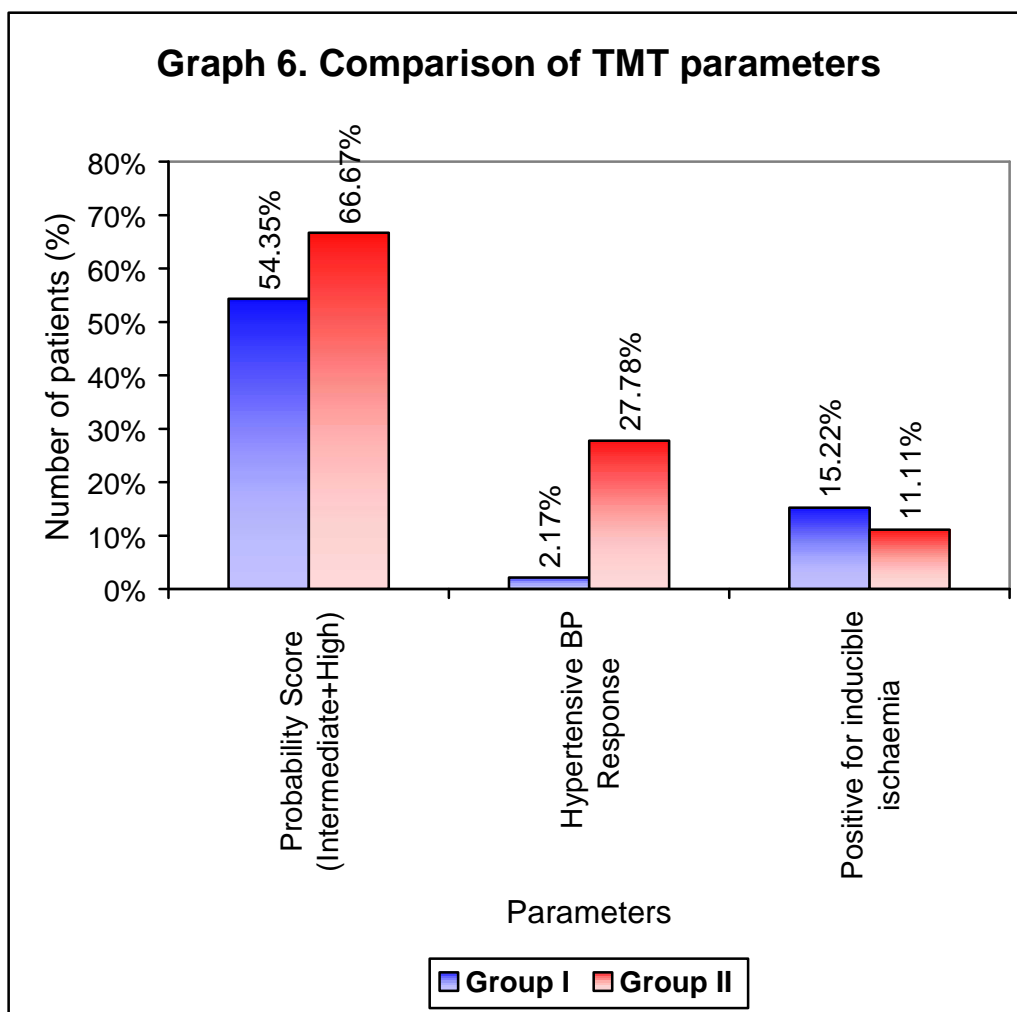
GFR was marginally lower ( $116.7 \pm 29.9$  ml/min) in Group II compared to Group I ( $121.0 \pm 26.5$  ml/min) however this was not statistically significant. Higher mean cholesterol levels ( $203.0 \pm 42.0$  mg/dL) was seen in Group II individuals than in Group I ( $178.7 \pm 34.2$  mg/dL) with significant ( $p=0.002$ ). LDL-C was also significantly higher in Group II ( $123.0 \pm 41.2$  mg/dL) as compared to Group I ( $107 \pm 35.03$  mg/dl) with significant ( $p=0.040$ ). Similarly TG levels were much higher ( $178.35 \pm 136.29$  mg/dL) in group II as compared to Group I ( $131.28 \pm 64.24$  mg/dL) which was statistically significant ( $p=0.027$ ). HDL levels also were lower in Group II ( $45.0 \pm 18.9$  mg/dL) as compared to Group I ( $46.32 \pm 20.03$  mg/dL). In nut shell higher cholesterol, LDL-C, TG and lower HDL-C; derangement of lipid profile increased with increasing blood pressure levels proposing it as one of risk factor for prehypertension and hypertension.

**Table 19. Comparison of Probability scores**

Probability scores	Group I (n=46)		Group II (n=54)		$\chi^2$	DF	P value
	No	%	No	%			
Low	21	45.65	18	33.33	1.585	1	0.208
Intermediate	20	43.48	26	48.15			
High	5	10.87	10	18.52			

**Table 20. Comparison of TMT parameters**

TMT Parameters	Group I (n=46)		Group II (n=54)		Z score	p value
	No	%	No	%		
HR recovery time Blunted	3	6.52	2	3.70	0.64	>0.05
Positive hypertensive BP response	1	2.17	15	27.78	3.48	<0.001
Positive inducible ischaemia	7	15.22	6	11.11	0.61	>0.05



Based on simple exercise test score, angiographic CAD probability; intermediate and high was seen more (66.67%) in Group II as compared to Group I (54.34%) indicating higher risk in Group II compared to group I although P value was not statistically very significant. This may be because of relatively small sample size.

In the present study hypertensive BP response indicating progression to HTN was seen more (27.78%) in Group II compared with Group I (2.17%) and these findings were statistically significant ( $p < 0.001$ ). Patients in both the groups

had almost similar rates of positivity for inducible ischemia indicating that both Group I and II are at increased risk of IHD.

**Table 21. Comparison of diabetic, prediabetic and non diabetic prehypertensive**

Parameters	DM		Pre Diabetes		Non Diabetics		p value
	Mean	SD	Mean	SD	Mean	SD	
Basal heart rate	85.79	9.42	84.9	11.04	79.71	9.98	a 0.762 b 0.010 c 0.056
BMI	26.09	3.89	26.82	4.17	25.43	3.88	a 0.531 b 0.472 c 0.118
WHR	0.85	0.05	0.85	0.04	0.84	0.06	a 1.000 b 0.456 c 0.413
Mean SBP	131.2	5.83	132.6	4.87	128.2	5.53	a 0.377 b 0.026 c 0.002
Mean DBP	84.75	3.87	84.5	4.01	82.39	3.57	a 0.827 b 0.008 c 0.031
GFR	111.7	32.67	120.8	23.1	121.7	27.64	a 0.282 b 0.154 c 0.896
Cholesterol	191.3	51.02	187	37.7	194.1	35.06	a 0.747 b 0.797 c 0.447
LDL	119	45.01	114.3	39.65	114.3	36.09	a 0.705 b 0.614 c 1.000
HDL	41.39	7.52	44.1	14.47	48.55	24.69	a 0.440 b 0.060 c 0.346
TG	157.5	78.66	198.00	199.70	139.3	64.76	a 0.387 b 0.272 c 0.201

Diabetic vs prediabetic = a, Diabetic vs non diabetic = b, Prediabetic vs non diabetic = c

Mean basal heart rate of diabetic prehypertensives was marginally more (85.79 ± 9.42 beats/min) as compared to Prediabetic prehypertensives (84.9 ± 11.04 beats/min). But Heart rate in diabetic and prediabetic both were

significantly higher  $85.79 \pm 9.42$  beats/min and  $84.9 \pm 11.04$  beats/min respectively as compared to nondiabetic prehypertensive ( $79.71 \pm 9.98$  beats/min) ( $p=0.010$ ) for diabetics and non diabetics.

As autonomic dysfunction, sympathetic overactivity is proposed mechanism for prehypertension and increased basal heart rate these findings indicated that autonomic dysfunction may be increased due to diabetic/prediabetic status.

There was not much change in BMI and WHR with blood sugar levels (diabetic status).

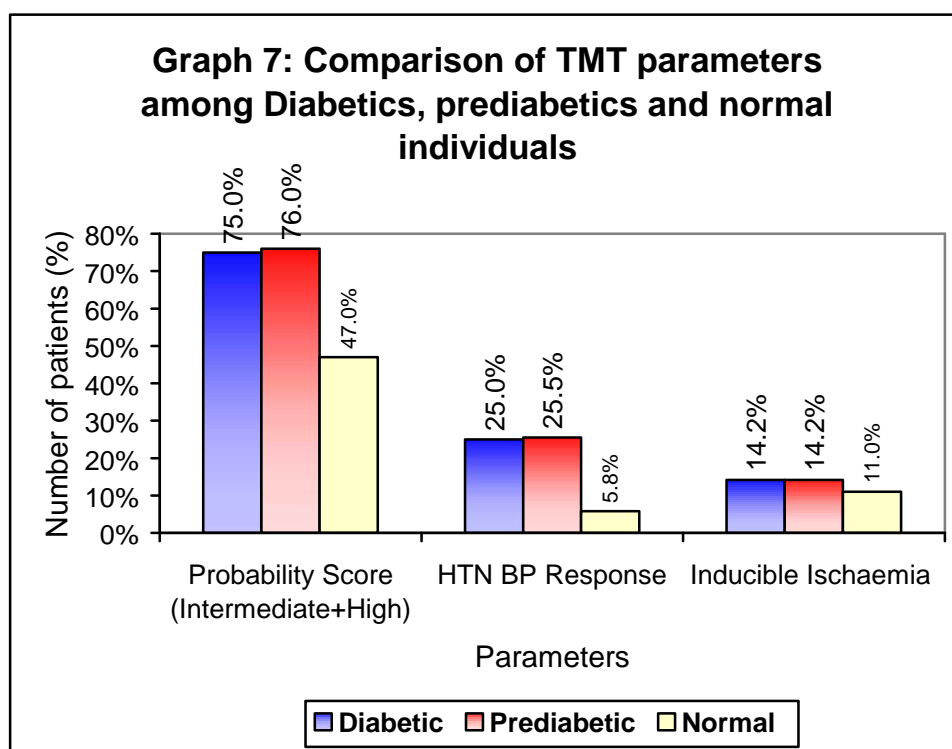
Mean SBP and Mean DBP was higher in diabetic and prediabetic individuals ( $131.2 \pm 5.83$  mm Hg,  $132.6 \pm 4.87$  mm Hg) and ( $84.75 \pm 3.87$  mm Hg and  $84.5 \pm 4.01$  mm Hg) as compared to non diabetic individuals ( $128.2 \pm 5.53$  mm Hg and  $82.39 \pm 3.57$  mm Hg) with significant p value 0.026 (SBP of DM – Non DM); 0.002 (SBP Prediab – Non DM) and significant p value of 0.008 (DBP of DM – Non DM); 0.031 (DBP Prediab – Non DM). Proposing diabetes/prediabetes as a risk factor for prehypertension.

There was marginal decrease in GFR in diabetic prehypertensives as compared to non diabetic prehypertensives, however this decrease in GFR was statistically not significant ( $p=0.282$ ).

There was not much difference in lipid profile of diabetic, prediabetic and non diabetic. But these were deranged as compared to normal population indicating deranged lipid profile as one of risk factor for prehypertension.

**Table 22. Comparison of TMT finding in diabetic, pre diabetic and non diabetic prehypertensives.**

Parameters	DM (n=28)		Pre DM (n=21)		Normal (n=51)		$\chi^2$	DF	P
	No	%	No	%	No	%			
<b>Probability Scores</b>									
Low	7	25.0	5	23.8	27	52.9	8.510	2	0.014
Intermediate	15	53.5	12	57.1	19	37.2			
High	6	21.4	4	19.0	5	9.8			
<b>Heart Rate Recovery time</b>									
Blunted	1	3.5	0	0	4	7.8	-	-	-
<b>Hypertensive BP response</b>									
Positive	7	25.0	6	28.6	3	5.8	8.041	2	0.018
<b>Inducible ischaemia</b>									
Positive	4	14.2	3	14.2	6	11.7	0.140	2	0.932



Among all prehypertensives, diabetics and prediabetics are at more risk for intermediate and high angiographic CAD probability 75% and 76% respectively as compared to 47% with non diabetic prehypertensives with statistically significant P value of 0.014, indicating that both diabetes, prediabetes as well as prehypertension are risk factors for CAD or among prehypertensives also diabetic and prediabetics are at increased risk for CAD.

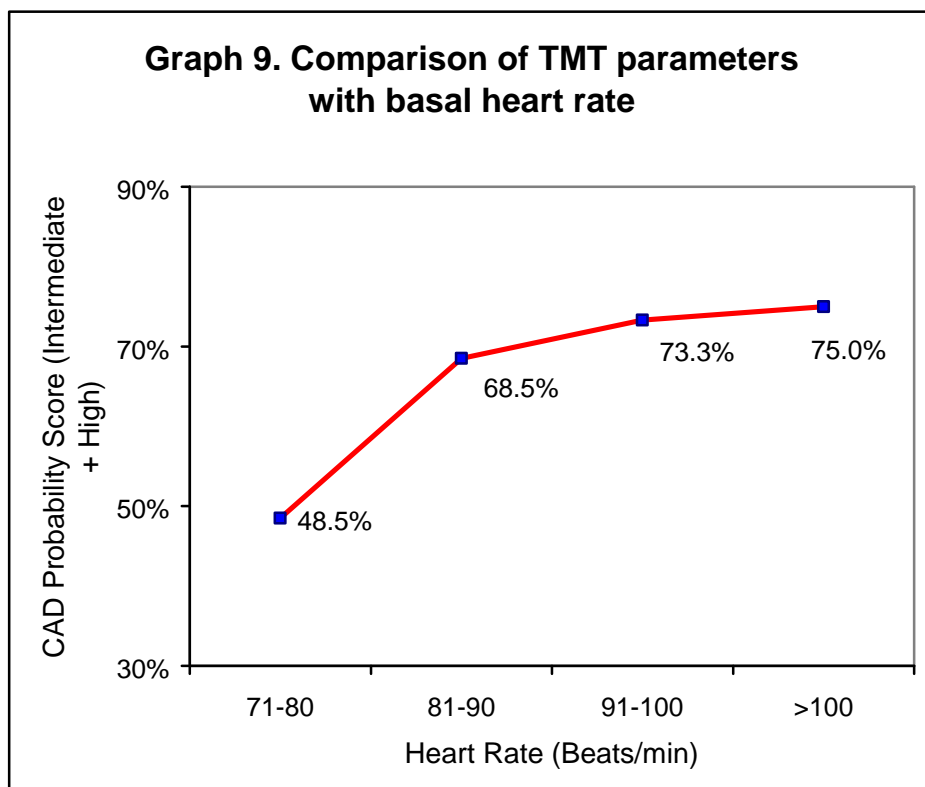
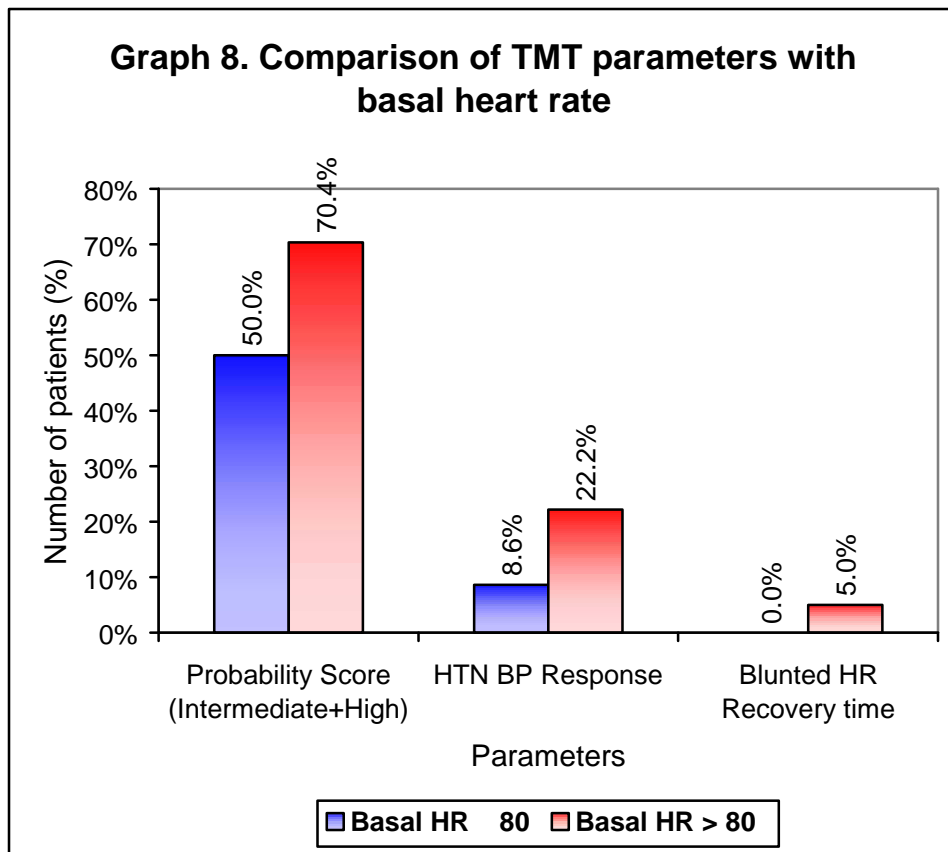
Hypertensive BP response was seen more commonly in Diabetics and prediabetic (25%, 25.5%) as compared to 5.8% seen with non diabetic prehypertensives (p=0.014) indicating that risk of progressing to hypertension is much more higher in diabetics and prediabetics.

TMT showed positive for inducible ischaemia result in 14% DM, 14.2% prediabetic and 11% non DM individuals. However this was not statistically significant (p=0.932).

This indicated that current ischaemic heart disease was present almost equally in all 3 groups. But future angiographic CAD probability worsened (increased) with increasing glycemic status. Thus diabetes or prediabetes in association with prehypertension is as an early predictor of CAD.

**Table 23. Comparison of TMT Parameters with basal heart rate among prehypertensives**

Parameters	HR 80 (n=46)				HR > 80 (n=54)					
	60 – 70 (n=13)		71-80 (n=33)		81-90 (n=35)		91-100 (n=15)		>100 (n=4)	
	No	%	No	%	No	%	No	%	No	%
<i>Probability Scores</i>										
Low	6	46.1	17	51.5	11	31.4	4	26.6	1	25.0
Intermediate	5	38.4	13	39.9	17	48.5	9	60.0	2	50.0
High	2	15.3	3	9.09	7	20.0	2	13.3	1	25.0
<i>Heart Rate Recovery time</i>										
Blunted	0	0	0	0	3	8.5	2	13.3	0	0
<i>Hypertensive BP response</i>										
Positive	1	7.69	3	9.09	8	22.8	4	26.6	0	0
<i>Inducible ischaemia</i>										
Positive	2	15.3	4	12.1	6	17.1	1	6.6	0	0



Out of 100, 46% had basal heart rate less than or equal to 80 beats/min and 54% had HR more than 80 beats/min. 70.37% individuals with HR more than 80 beats/min had intermediate and high probability which was much more than those with HR less than or equal to 80 beats/min (50%) ( $p=0.037$ ). As heart rate increased from 71 to 80, 81 to 90, 91 to 100, more than 100 beats/min, CAD probability increased steadily from 48.5%, 68.5%, 73.3% and 75% indicating more the basal heart rate more the angiographic CAD probability. This indicated that increased basal Heart Rate more than 80 beats/min in association with prehypertension was associated with increased CAD probability as compared to lower basal heart rate.

Similarly hypertensive blood pressure response was seen much higher (22.2%) in people with basal HR more than 80 beats/min as compared to (8.6%) in HR less than or equal to 80 beats/min ( $p=0.06$ ) showing that heart rate in relation to prehypertension is an important predictor of progression to hypertension in future.

All 5% patients with blunted heart rate recovery time were having their basal heart rate more than 80 beats/min with significant p value.

**Table 24. Association of variables with change in delta 30 mm Hg**

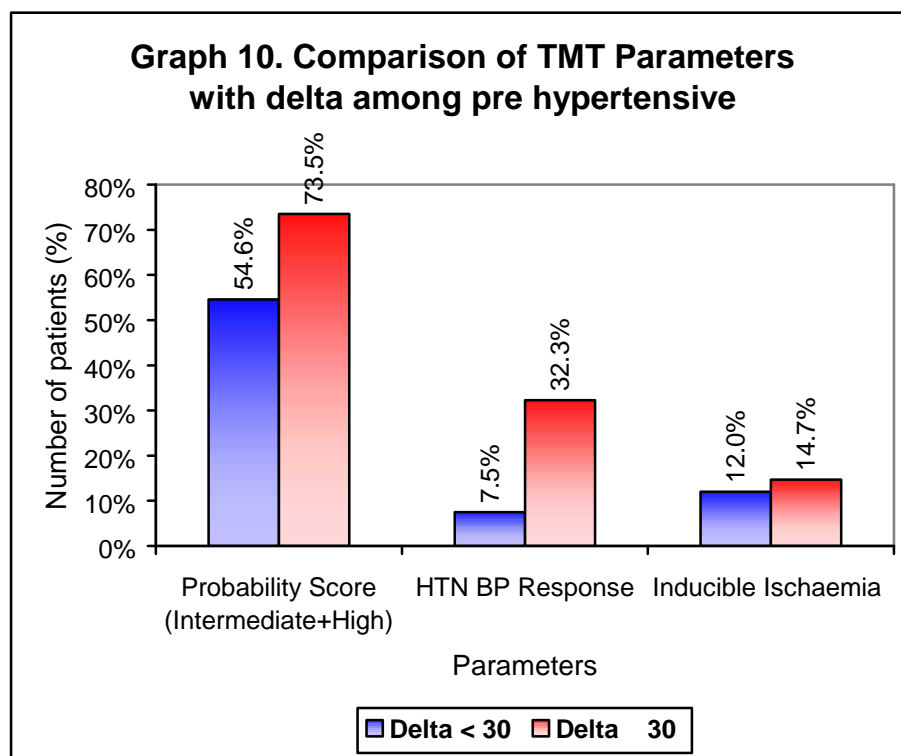
Demographic and Clinical Parameters	Group 1 (n = 66) delta < 30		Group 2 (n = 34) delta ≥ 30		t	DF	P
	Mean	SD	Mean	SD			
Age	45.23	9.66	49.91	9.24	2.329	98	0.022
BMI	26.01	4.27	25.71	3.28	0.390	98	0.698
WHR	0.85	0.06	0.85	0.05	0	98	1
Pulse rate	82.18	10.76	83.12	9.68	0.428	98	0.670
<b>Laboratory profile</b>							
GFR	125.3	26.81	105.86	27.18	3.419	98	0.001
Cholesterol	195.8	44.29	184.18	30.34	1.542	98	0.127
LDL	119.18	43.04	108.74	29.57	1.424	98	0.158
HDL	45.88	20.15	45.09	18.06	0.192	98	0.848
TG	161.95	126.68	146.5	73.21	0.772	98	0.442

Mean age of group of patients having any stage more than or equal to 30 mm of Hg was  $49.91 \pm 9.24$  years which was higher as compared to  $45.23 \pm 9.66$  years in patients with less than 30; p value (0.02) significant, indicating more than 30 parameter increases with increasing age. Basal Heart Rate, BMI, WHR there was no significant difference in both the groups less than 30 or more than or equal to 30.

GFR was lower ( $105.8 \pm 27.1$  ml/min) in group with more than or equal to 30 as compared to  $125.3 \pm 26.8$  ml/min in group with less than 30, (p=0.001). There was not much difference between two groups in their lipid profile.

**Table 25. Comparison of TMT Parameters with delta among pre hypertensives**

Parameters	Group 1 ( less than 30 mm Hg) (n=66)		Group 2 ( more than or equal to 30 mm Hg) (n=34)	
	No	%	No	%
<i>Probability Scores</i>				
Low	30	45.5	9	26.4
Intermediate	27	40.9	19	55.8
High	9	13.6	6	17.6
	$\chi^2=3.399$ DF=1 p=0.065			
<i>Heart Rate Recovery time</i>				
Blunted	3	4.54	2	5.8
	Z=0.32 p>0.5			
<i>Hypertensive BP response</i>				
Positive	5	7.57	11	32.3
	Z=3.20 p<0.005			
<i>Inducible ischaemia</i>				
Positive	8	12.1	5	14.7
	Z=0.37 p>0.5			



Group II ( $n = 30$ ) was associated with more (73.5%) (high 17.6% and intermediate 55.9%) CAD Probability as compared to (54.55%) in Group I (high 13.6%, intermediate 40.9%) ( $p=0.065$ ). Hypertensive BP response was seen more commonly (32.3%) as compared to Group I (7.5%) ( $p<0.005$ ) showing that those with any stage more than 30 mm of Hg were at more than four times increased risk for developing hypertension than those with less than 30 mm Hg. TMT was also positive for inducible ischaemia more in Group II (14.7%) as compared to Group I (12%). Heart rate recovery time was also seen more blunted (5.9%) in group 2 as compared to (4.5%) in Group I. However these both were not statistically very significant.

**Table 26. TMT Parameters among prehypertensives with stage 2 BP more than 180/90 (n=17)**

Parameters	Stage 2 BP > 180/90 mm Hg	
	Number	Percentage (%)
<i>Probability Scores</i>		
Low	3	17.64
Intermediate	11	64.70
High	3	17.64
<i>Heart Rate Recovery time</i>		
Blunted	2	11.76
Hypertensive BP response		
Positive	9	52.94
<i>Inducible ischaemia</i>		
Positive	2	11.76

Another parameter stage 2 BP more than 180/90 according to some studies is an important predictor of CAD in future. In the present study total 17 patients had stage 2 BP more than 180/90. 82% of them had intermediate and high CAD probability using simple exercise test score. 12% had blunted heart rate recovery time. Hypertensive blood pressure response was seen in 53% of patients. TMT of 12% were positive for inducible ischaemia. These all things demonstrate that TMT parameter stage 2 BP >180-90 helps us to delineate individuals with much higher CAD probability (82%) and hypertensive BP response (53%) indicating that CAD probability is higher in these individuals. Progression to HTN is much more in these individuals and autonomic dysfunction indicated by blunted heart rate response was also much more common in those individuals when compared to other prehypertensives in general.

## **DISCUSSION**

Prehypertension is a widely prevalent entity. Its relationship to various risk factors like age, smoking, family history of hypertension, diabetes, prediabetes, obesity and dyslipidemia have been stated in various studies.

We conducted a study on 100 prehypertensive individuals to establish the role of various risk factors and determine the factors affecting their future cardiovascular risk.

The 100 prehypertensives were selected randomly using random number table and they were subjected to thorough clinical examination as well as various laboratory tests and tread mill test.

In the present study there were 87% males and 13% females with a majority of patients being in the age group of 41 to 60 years (72%), 5% individuals were more than 60 years. The prevalence of prehypertension decreased in the above 60 years age group probably because of higher prevalence of hypertension in older age group.<sup>16</sup>

Family history of diabetes was seen in 35% individuals and family history of hypertension was seen in 34% individuals indicating that family history is an important risk factor for prehypertension.

Similar studies done on Chinese population also showed the role of family history of hypertension as a risk factor for prehypertension.<sup>57</sup>

In this study there were 25% smokers and 21% alcoholics. This may suggest smoking as a risk factor for prehypertension. However in the study done on prediabetic Omani population history of smoking was comparatively less 13%,<sup>58</sup> while it was way more 42% in a study done on 6859 participants of Framingham heart study.<sup>12</sup>

In the present study, the mean BMI was  $25.91 \pm 9.35$  kg/m<sup>2</sup> and 61% patients were either over weight (46%) or obese (15%). In another study conducted on Western individuals, it was shown that 70% patients were either obese or overweight and there were more obese (40%) compared to overweight (30%).<sup>59</sup> The BMI is an important risk factor and strongest predictor of prehypertension which has been proved by various studies.<sup>19,22,23</sup>

The findings of present study also suggest BMI more than 25 kg/m<sup>2</sup> as an important risk factor as well as determinant of prehypertension.

Higher basal heart rate (more than 80 beats/min) has been cited in various studies in relation to prehypertension. In our study mean Basal Heart Rate was  $82.50 \pm 10.37$  beats/min and 54% individuals were having their basal heart rate more than 80 beats/min.

These figures were much more higher and astonishing than previous studies like in Atherosclerosis risk in communities (ARIC) study where only 13.1% patients were having their Basal heart Rate more than 80.<sup>8</sup>

These may suggest a cause/effect relationship of basal heart rate and prehypertension and may propose that increased basal heart rate is a risk factor

for prehypertension. This may also implicate common etiology that is, sympathetic overactivity, hormonal mechanisms and psychoneuronal processes that reflect increase stress/anxiety for both, increased basal heart rate and prehypertension.

Prehypertensives having basal heart rate more than 80 beats/min had significantly higher CAD probability (intermediate + High; 70.37%) score calculated from simple exercise test score than those with basal heart rate less than 80 beats/min (probability score 50%) (p=0.037).

This parameter helps us in better future CAD prediction and our results are in line with ARIC study which calculated CAD risk and mortality prospectively in patients with basal heart rate more than 80 beats/min.<sup>8</sup>

Similarly as heart rate increased from (71 to 80), (81 to 90), (91 to 100) and more than 100; CAD probability increased steadily from 48.5%, 68.5%, 73.3%, 75% respectively emphasizing the effect of heart rate on cardiovascular risk.

Hypertensive BP response on TMT which is a predictor of development of future hypertension was seen almost three times (22.2%) in people with basal heart rate more than 80 beats/min than, (8.69%) in people with basal heart rate less than 80 beats/min.

In our study 5% of all prehypertensives were having blunted heart rate recovery time response, which is a good marker of autonomic dysfunction (increased sympathetic activity and decreased parasympathetic release).

Interestingly all these 5% subjects were having basal heart rate more than 80 beats/min.

Thus all these parameters denote that basal heart rate is an important parameter in prehypertensives and brings to light the common etiology and its various adverse effects in prehypertensives like progression to hypertension, CVD risk and autonomic dysfunction. Possible mechanisms explaining these findings are;

- 1) Increased sympathetic tone
- 2) Hormonal mechanisms
- 3) Psychoneuronal processes that reflect increase stress/anxiety.

Increased sympathetic activity causes increased heart rate and also has been associated with atherosclerosis and development of heart failure.<sup>60,61</sup>

Increased stress and anxiety which often stimulate sympathetic activity are well documented additive risks for people with prehypertension and may play role in its original development.<sup>60,62,63</sup> Further evidence suggests that, sympathetic activity plays a role is that, anxiety is often accompanied by increased heart rate and lowering heart rate intentionally, through non pharmacologic strategies like meditation may reduce cardiovascular risk.

Increased sympathetic tone or anxiety reflected in an elevated heart rate and prehypertension may be an early warning of increased cardiovascular risk and may accelerate development of hypertension and atherosclerosis.

In this study diabetes and prediabetes were diagnosed based on ADA criteria, prevalence of diabetes and prediabetes was (28%) and (21%) respectively. Diabetes prevalence in this study was quite high when compared to previous studies like ARIC study where prevalence was 6.5%.<sup>8</sup>

However prediabetes in relation to prehypertension was almost similar (21.6%) in a study done on Omani population.<sup>58</sup>

High prevalence of diabetes mellitus in our study may be explained on the basis of increased chances of prehypertension being detected in diabetics as they have more frequent visits to health care professionals.

This explains diabetes as well as prediabetes as a risk factor for prehypertension. It is also a known fact that prehypertensives are more likely to have diabetes and prediabetes.<sup>21,22</sup>

Dyslipidemia is a risk factor for prehypertension. The lipid profile of all 100 prehypertensives was done and evaluated based on ATEP III guidelines.

In this study 32% subjects were having serum cholesterol more than 200 mg/dL, LDL-C (more than 130 mg/dL) was seen in 31% and hypertriglyceridemia (TG more than 150 mg/dL) was seen in 37% prehypertensives. The HDL-C was lower than 40 mg/dL in 54% individuals.

Studies done in Israel suggest, hypercholesteremia,<sup>16,23</sup> increased LDL-C, increased TG,<sup>19</sup> low HDL-C<sup>19</sup> are seen more commonly with prehypertensives than normotensives.<sup>22</sup> Hence the role of statins in prehypertensives needs to be evaluated.

Based on risk factors like obesity, diabetes and dyslipidemia it is suggested that metabolic syndrome as a whole is a risk factor for prehypertension.<sup>23</sup>

Glomerular filtration rate, a marker of target organ damage was less than 90 ml/min in 17% of prehypertensives. Out of them 9% were diabetics, 2% prediabetics and 6% were non diabetics. Diabetes and prediabetes is known to be associated with decreased GFR but this data indicates that non diabetic prehypertensives are also at risk for development of target organ damage.

After all these baseline characteristics and laboratory parameters, tread mill test was done for all 100 prehypertensives and it was seen that a total of 61% subjects had intermediate and high probability for CAD based on simple exercise test score. These results were quite alarming and as such there are not many studies done based on simple exercise test score for comparison.

Similarly TMT of 13% individuals was positive for inducible ischaemia, indicating that they could have IHD which is quite high when compared to general population.

Hypertensive BP response that is SBP more than 210 in males and more than 190 females was seen in 16% of prehypertensives indicating the increased probability of progressing to hypertension in the near future.

Heart rate recovery time which is a measure of autonomic dysfunction; was blunted or abnormal in 5% prehypertensives and most of these individuals

were nondiabetic indicating that autonomic disturbance is an important pathophysiology for prehypertension irrespective of diabetic status.

Further prehypertensives were classified into two groups. Group I with BP 120-129/80-84 mm Hg and Group II with BP 130-139/85-89 mm Hg and compared both the groups.

Mean age in group II was  $48.46 \pm 9.39$  years, higher than group I ( $44.89 \pm 9.87$  years) again indicating that prehypertension increases with age and also level of prehypertension is more with increasing age.

Similarly BMI and WHR and dyslipidemia also increased from Group I to Group II indicating both as a risk factor and helps us stating the fact that “prehypertension is a marker of deranged cardiometabolic profile” as stated in the literature.<sup>64</sup>

In another study done on 6859 participants of Framingham Heart study, it was found that age was more in Group II also called as high normal ( $51 \pm 2$  years) than Group I ( $49 \pm 2$  years). Similarly BMI also increased from optimal ( $25 \pm 3.5$ ) to normal ( $26 \pm 3.3$ ) and to high normal ( $26.7 \pm 3.5$ ) group.<sup>59</sup>

High prevalence of diabetes mellitus and hypercholesteremia was also seen in high normal group (Group II in this study).

In this study mean basal heart rate was more in group II ( $84.4 \pm 10.48$  beats/min) compared to Group I ( $80.26 \pm 9.87$  beats/min) suggesting common etiology of sympathetic over activity and parasympathetic under activity.

When TMT parameters were compared between two groups, CAD probability (intermediate + high) was almost 12% higher in Group II than in Group I, though this was not statistically significant.

Hypertensive BP response predicting future hypertension was present almost 14 times higher in Group II than in Group I with significant P value < 0.001.

Hence group II, previously called as high normal group, has more derangement of lipid profile, increased basal heart rate, more BMI, increased WHR, increased risk of future CAD and very high chances of progression to hypertension compared to Group I. Hence pharmacologic treatment of this group of prehypertensives should be considered.

Further the patients were analyzed on basis of diabetic status. In this study there were 28% diabetics, 21% prediabetics and 51% were having normal blood sugar levels.

Mean basal heart rate statistically increased from nondiabetic ( $79.71 \pm 9.98$  beats/min) to prediabetic ( $84.9 \pm 11.04$  beats/min) and further to diabetic ( $85.79 \pm 9.42$  beats/min) ( $p=0.010$ ).

This can be explained by virtue of diabetes causing autonomic dysfunction which is the etiology for increased basal heart rate.

Mean SBP and DBP was significantly higher in diabetics and prediabetics than non diabetics indicating diabetes as well as prediabetes as a risk factor for prehypertension.

In the present study other metabolic parameters like lipid profile, BMI and WHR did not vary much between three groups.

TMT parameters like CAD probability and hypertensive BP response was also much higher in diabetic and prediabetic than nondiabetic.

There was not much difference between diabetic and predibetic groups in all aspects and both groups should be considered equally as important risk factor for CVD and progression to HTN.

Hypertensive BP response according to some studies was defined as any stage change in BP that is delta more than 55 mm Hg, but in this study there were hardly any individuals having delta more than 55 mm Hg. Hence any stage change in BP by delta more than or equal to 30 mm Hg was considered and subjects were categorized into two groups namely Group 1, with delta less than 30 mm Hg and Group 2 with delta more than or equal to 30 mm Hg.

Group 1 had 66 individuals and Group 2 had 34 individuals. TMT parameters like angiographic CAD was almost 20% more in Group 2 compared to Group 1.

Similarly hypertensive BP response in Group II (32.59%) was almost four times Group I (7.5%) showing that prehypertensives having any stage delta more than or equal to 30 mm Hg were more at risk for progression to hypertension.

According to a recent study stage 2 TMT BP more than 180/90 mm Hg is an important risk factor for CVD death in normotensives and prehypertensive individuals.<sup>65</sup>

In this study 17% prehypertensives were having stage 2 BP more than 180/90 mm Hg. 82% of these had intermediate and high CAD probability which was way high than any group among prehypertensives.

Similarly 52% subjects had hypertensive BP response which is also quite high. This indicates that those patients among prehypertensives having stage 2 BP more than 180/90 mm Hg are at highest risk for future CVD and progression to hypertension.

The limitations of the study were;

- The findings of the above study could not be compared with normal and hypertensive individuals.
- The study design was one year cross sectional study but to definitely prove angiographic CAD probability either coronary angiography or follow-up should have been done.
- Also the present study was a hospital based study but for better results study design should have been community based study.
- In this study GFR was considered as a marker for target organ damage instead of which microalbumuria would have been a better marker.

From the present study it can be well documented that high normal BP group (130-139/85-89 mm Hg) had much higher risk than other prehypertensives hence this group should be proposed for treatment among prehypertensives. Presence of prehypertension should be considered as a stage of deranged cardio

metabolic profile and should be taken seriously. Not only diabetes, prediabetics also should be considered for treatment in high normal group.

Increased basal heart rate more than 80 beats/min is an important risk factor and in association with prehypertension has been associated with adverse cardiometabolic profile.

Till now only ACE inhibitors are drugs under trial for prehypertension. But based on these findings  $\beta$ -Blockers should be evaluated in clinical trials for treatment of prehypertension especially in prehypertensives with basal heart rate more than 80 beats/min.

The TMT is an important tool for future prediction hence advisable to be done on all prehypertensive individuals.

Prehypertensives with any stage delta more than or equal to 30 mm Hg forms an important risk group for progression to hypertension and CVD risk. Hence, these individuals should be targeted earliest. Stage 2 BP more than 180/90 mm Hg is an important predictor of future hypertension and coronary artery disease. It helps in identifying individuals among prehypertensives who need to be targeted upon earliest.

## **CONCLUSION**

The number of people with prehypertension is substantial and this is increasing worldwide. The continuous relationship of blood pressure to cardiovascular outcomes and high rate of progression from prehypertension to hypertension is strongest support for a more aggressive approach to treat prehypertension.

The present study proved the association of prehypertension with various risk factors like advancing age, smoking, family history of hypertension.

Obesity, dyslipidemia and basal heart rate of more than 80 beats/min formed an important risk factors, as well as determinants of prehypertension, as they all increased with the increasing levels of blood pressure even among prehypertensives.

The TMT evaluation of prehypertensives helps us to predict future cardiovascular disease probability and progression to hypertension based on simple exercise test score (for CAD probability) and hypertensive BP response respectively. Parameters like high normal BP, diabetic / prediabetic status, basal heart rate more than 80 beats/min, any stage delta more than 30 mm Hg and stage 2 BP more than 180/90 mm Hg are at increased risk of future CVD and progression to hypertension.

This evidence is enough to evaluate the efficacy of antihypertensive treatment for prehypertensive patients in clinical trials, particular in selected patients.

## SUMMARY

Cardiovascular disease is still on the increase in India owing to changing socioeconomic factors and unhealthy lifestyles. Better understanding of the role of HTN has led to new JNC-7 guidelines for its diagnosis and management. The present study was aimed to establish correlation between prehypertension and various other facts like obesity, diabetes, cardiovascular disorders and target organ damages.

The present one year cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 100 patients with prehypertension during the period of January 2009 to December 2009. Demographic data like gender and age were collected along with relevant history and a thorough clinical examination was conducted and the findings were recorded. Three BP readings, five minutes apart were taken and mean of second and third reading was selected as a final blood pressure. Special tests such as renal functional tests (serum creatinine), Lipid Profile, Tread Mill Test and fundoscopy were conducted and recorded.

In this study out of 100 prehypertensives, majority were males (83%) and aged between 41 to 50 years (39%) followed by 51 to 60 years (33%). Majority (61%) patients were overweight and obese, with overall mean basal heart rate of  $82.50 \pm 10.37$  beats/min and 28% were diabetics and 21% were prediabetics. Angiographic coronary artery disease probability calculated by simple exercise test score showed majority (61%) having; intermediate (46%) and high (15%) probability and (39%) subjects had low probability for angiographic CAD. TMT

showed positive for inducible ischaemia in 13% subjects. Hypertensive BP response (SBP >210 mmHg in males and >190 mmHg in females) was seen in 16% subjects. Heart rate recovery time blunted which is marker of autonomic dysfunction was seen in 5% of prehypertensives.

Age, smoking, family history, prediabetes and diabetes are the important risk factors for prehypertension. The obesity, dyslipidemia and basal heart rate of more than 80 beats/min formed an important risk factors, as well as determinants of prehypertension. Prehypertensives are at increased risk for cardiovascular disease and progression to hypertension.

Similarly high normal BP, diabetic or prediabetic status, TMT any stage delta more than or equal to 30 mm Hg and stage 2 BP more than 180 / 90 mm Hg are at increased risk of future CVD and progression to hypertension.

These parameters help us to define high risk individuals among prehypertensives so that the treatment strategies can be formed or revised for these group of individuals.

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## **ANNEXURE I - CONSENT FORM**

### **“CLINICAL AND LABORATORY PROFILE OF PREHYPERTENSION IN ADULTS – A ONE YEAR CROSS-SECTIONAL STUDY”**

#### **Objective and purpose of the study**

This research is intended to study clinical and laboratory profile of prehypertensives and find correlation between other conditions like diabetes, obesity, coronary artery disease, end organ damage. The principal investigator of the study is Dr. \*\*\*\* \* under the guidance of Dr. \*\*\*\*\*. My co-operation will be of great help to patients with prehypertension in future.

#### **Procedure**

If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood samples and undergo other necessary investigations

#### **Risk and Benefits**

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations which may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn and other complications during TMT (rarely happens).

### **Alternatives**

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study any time. If you choose not to take part in the study you will receive the standard treatment for patients with your condition.

### **Privacy and Confidentiality**

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

### **Institution / Sponsor's policy**

Does not apply to this research

### **Financial incentives for participation**

You will not be paid / offered any gifts /incentives for participating in the study.

### **Authorization to publish the results**

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MS degree, review and publishing.

If you have any questions about my rights as a participant you may call  
Chairman, J.N.M.C Ethical Committee for Human Research.

In case of the queries during study or in future you may contact following person

Principal investigator : Dr. \*\*\*\*\* \*\*\*\*\*

Guide : Dr. \*\*\*\*\* \*\*\*\*\*

### **Consent Statement**

I voluntarily agree to take part in this study by signing below. I may  
withdraw at any time. I am not giving up any of my legal rights by signing this  
form. My signature below indicates that I have read, or it has been read to me,  
this entire consent form, and have had all my questions answered.

Name of the Participant: \_\_\_\_\_ Signature \_\_\_\_\_  
/ Thumb print

Name of the Witness; \_\_\_\_\_ Signature \_\_\_\_\_

Investigator Name \_\_\_\_\_ Signature \_\_\_\_\_

Date:

Place:

**ANNEXURE II – PROFOMA**

Patient Name: I.P/O.P number:  
Age: Sex:  
Date of admission: Date of discharge:  
Address:

**Presenting complaints**

**Present History**

History suggestive of;

Diabetes mellitus :  
Hypertension :  
Ischaemic heart disease :

**Past History**

**Family History** DM / HTN / IHD / Obesity

No. of siblings

Health status of siblings

**Personal history**

Smoking :  
Exercise :  
Alcohol intake :

Tobacco chewing :

Any other :

**Treatment History**

**General Physical Examination**

Built and nourishment:

Pulse :

Peripheral pulses :

**Blood pressure** :      **1.**                      **2.**                      **3.**

Mean of 2<sup>nd</sup> & 3<sup>rd</sup> reading:

Anthropometry :

Height (Cms) :                                      Weight(Kg) :

Hip girth (Cms) :                                      Waist girth (Cms) :

Waist hip ratio :

BMI :

**Systemic examination**

CVS :

RS :

Per abdomen :

CNS :

**Investigations**

**Haemogram**

Hb% :

TC :

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DC	:	N -	M -	E -
B -				
ESR	:			
Blood Sugar				
FBS	:		PPBS	:
Serum creatinine	:			
GFR	:			
Lipid profile				
Cholesterol	:			
LDL	:			
HDL	:			
TG	:			
Fundoscopy	:			
Heart rate	:			
Blood group	:			

## Tread mill test

Variable	Circle response	Sum	
Maximal heart rate	< 100 bpm = 30		<b>Men</b> <b>&lt; 40 = Low</b> <b>probability</b>  <b>40 – 60</b> <b>Intermediate</b> <b>Probability</b>  <b>&gt; 60 = High</b> <b>probability</b>
	100 to 129 bpm = 24		
	130 to 159 bpm = 18		
	160 to 189 bpm = 12		
	190 to 220 bpm = 6		
Exercise ST depression	1 – 2 mm = 15		
	> 2 mm = 25		
Age	> 55 Years = 20		
	40 to 55 years = 12		
Angina History	Definite typical = 5		
	Probable atypical = 3		
	Non cardiac pain = 1		
Hypercholesteromia ?	Yes = 5		
Diabetes	Yes = 5		
Exercise test induced angina	Occurred = 3		
	Reason for stopping = 5		
	Total score		

Variable	Circle response	Sum	
Maximal heart rate	< 100 bpm = 20		<b>Women</b>
	100 to 129 bpm = 16		
	130 to 159 bpm = 12		
	160 to 189 bpm = 8		
	190 to 220 bpm = 4		
Exercise ST depression	1 – 2 mm = 6		<b>&lt; 37 = Low probability</b>
	> 2 mm = 10		
Age	> 55 Years = 25		<b>37 – 57</b>
	40 to 55 years = 15		
Angina History	Definite typical = 10		<b>Intermediate Probability</b>
	Probable atypical = 6		
	Non cardiac pain = 2		
Hypercholesteromia ?	Yes = 10		<b>&gt; 57 = High probability</b>
Diabetes	Yes = 10		
Exercise test induced angina ?	Occurred = 9		
	Reason for stopping = 15		
Estrogen status	Positive = - 5, Negative = + 5		
	Total score		

# MASTER CHART

Sr. No.	O. P. No.	mograph		History						Anthropometry										General Physical Examination										Investigations																												
		Age (Years)	Sex	DM	IHD	HTN	IHD	Smoking	Alcohol	Height (Cms)	Weight (Kgs)	BMI (Kg/m2)	Waist (Cms)	Hip (Cms)	WHR	Pulse Rate (/Min)	BP reading (mm Hg)				Hb (gm%)	Sugar		Diabetic status	Sr. Creatinine (mg/dL)	GFR (ml/min)	Lipid profile				Resting						Tread Mill Test																					
																	1	2	3	Mean		FBS (mg/dL)	PPBS (mg/dL)				Cholesterol (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	TG (mg/dL)	BP (mm)		HR (min)	Stage 1		Stage 2		Stage 3																				
																															SBP	DBP		Delta	Delta	Delta	Delta	Delta	Delta																			
1	1244697	53	M	+	+	+	+	+	173	79	26.4	82	92	0.89	90	136	88	138	88	134	88	136	88	14.5	184	267	D	0.7	140	110	49	34	136	130	88	90	140	90	110	10	2	20	150	90	120	10	0	10	134	10.1	29	L						
2	1244699	57	M	+	+	+	+	+	167	78	27.97	90	102	0.88	72	130	80	138	90	134	88	136	89	15.5	139	167	D	1.1	83	301	211	62	188	130	89	74	140	90	114	10	1	40	150	90	134	10	0	20	160	90	151	10	0	17	151	10.1	66	H
3	1244188	57	M	+	+	+	+	+	165	69	21.67	77	88	0.88	110	130	80	128	80	132	80	130	80	15.4	171	240	D	1.3	52	189	92	37	298	130	80	112	140	80	126	10	0	14	150	80	144	10	0	18	160	80	165	10	0	21	165	10.0	57	I
4	1244700	46	F	-	-	-	-	-	157	60	24.34	82	97	0.85	82	120	80	122	80	124	80	123	80	13.7	92	102	N	0.7	96	189	123	42	119	120	80	110	130	80	154	10	0	44	150	80	169	20	0	15	150	80	176	0	0	7	176	10.1	29	L
5	1244754	57	M	+	+	+	+	+	167	74	26.53	82	94	0.87	92	130	80	122	80	134	88	128	84	14.6	86	75	N	1.1	78	164	81	38	226	130	80	112	150	80	152	20	0	40	180	90	174	30	0	22	180	90	182	0	0	8	182	10.1	53	I
6	1163236	52	F	-	-	-	-	-	154	72	30.36	90	106	0.85	96	140	90	138	80	138	88	138	84	13.4	129	159	PR	0.5	149	226	152	48	132	140	80	101	160	80	160	20	0	59	220	90	171	60	10	11	220	90	173	0	0	2	173	7.1	39	I
7	1163170	56	M	+	+	+	+	+	165	68	24.98	92	106	0.87	74	140	90	138	90	138	84	138	87	13.9	83	96	N	0.7	114	163	102	44	86	140	90	74	150	90	132	10	0	58	160	90	152	10	0	20	180	90	170	20	0	18	170	10.1	47	I
8	1238345	53	M	+	+	+	+	+	170	68	23.53	70	90	0.78	72	130	80	136	84	136	88	136	86	13.9	89	104	N	0.8	130	220	138	55	133	140	90	73	170	90	122	30	0	49	180	90	146	10	0	24	190	90	166	10	0	20	166	10.1	53	I
9	1238240	53	F	+	+	+	+	+	153	67	26.62	90	98	0.92	72	140	90	136	90	138	88	137	89	13.2	127	169	D	0.5	138	237	152	53	135	140	90	73	150	90	126	10	0	53	160	90	148	10	0	22	180	90	171	20	0	23	171	10.1	44	I
10	1213072	50	M	+	+	+	+	+	168	74	26.22	86	100	0.86	98	140	90	136	80	138	80	137	80	14.6	115	187	PR	0.7	140	191	127	33	154	140	80	100	150	80	115	10	0	15	180	80	130	30	0	15	190	80	157	10	0	27	157	10.1	45	I
11	1236038	45	M	+	+	+	+	+	173	79	26.4	82	92	0.89	84	140	90	138	88	138	88	138	88	16.6	97	114	N	1.1	95	227	160	48	97	140	90	88	150	100	136	10	0	48	200	100	151	50	0	15	210	100	164	10	0	13	164	10.1	44	I
12	1168904	43	M	+	+	+	+	+	165	73	26.81	90	96	0.94	72	120	80	130	80	130	80	125	80	15.4	100	133	N	1.0	102	165	103	41	104	110	80	73	130	80	112	20	0	39	150	80	123	20	0	11	160	80	150	10	0	27	150	10.2	30	L
13	1220517	59	M	+	+	+	+	+	178	99	31.25	97	104	0.93	88	130	90	132	88	130	80	131	84	15.9	118	126	D	0.9	123	123	61	42	100	130	90	89	140	90	146	10	0	57	150	90	162	10	0	16	160	90	179	10	0	17	179	10.1	60	H
14	1219768	64	M	+	+	+	+	+	172	93	31.44	84	97	0.87	84	130	80	124	80	130	84	127	82	16.2	91	108	N	0.6	104	176	120	43	67	120	80	66	130	80	127	10	0	61	160	80	155	30	0	28	180	80	162	20	0	7	162	8.4	63	H
15	1209501	52	M	+	+	+	+	+	171	75	25.65	84	94	0.89	86	120	80	124	84	124	84	124	84	13.9	142	188	N	0.9	136	141	85	37	82	120	80	68	130	80	92	10	0	24	140	90	115	10	0	23	150	90	142	10	0	27	142	10.1	65	H
16	1171521	48	F	-	-	-	-	-	154	55	23.19	86	96	0.9	78	120	80	120	82	124	82	122	82	13.0	98	76	N	0.4	144	201	126	53	112	130	80	69	150	80	144	20	0	75	160	80	150	10	0	6	170	80	169	10	0	19	169	10.2	29	L
17	1220506	43	M	+	+	+	+	+	167	90	30.27	96	104	0.92	84	130	80	130	80	134	80	132	80	14.5	125	131	PR	1.0	121	184	119	38	133	130	80	85	140	80	150	10	0	65	150	80	171	10	0	21	170	80	176	20	0	5	176	8.5	24	L
18	1209982	45	M	+	+	+	+	+	167	60	21.51	80	90	0.89	90	110	90	120	90	120	88	120	89	15.8	190	213	D	1.1	72	190	86	36	428	110	80	88	110	90	118	0	10	30	140	90	135	30	0	17	170	90	162	30	0	27	162	10.1	49	I
19	1209508	40	F	-	-	-	-	-	157	81	32.86	84	96	0.88	72	130	80	130	84	134	84	132	84	12.5	88	104	N	0.6	150	180	121	41	90	130	80	71	150	80	133	20	0	62	160	80	150	10	0	17	180	80	171	20	0	21	171	10.1	23	L
20	1166907	41	M	+	+	+	+	+	169	61	21.36	70	80	0.88	86	130	80	130	80	132	80	131	80	15.7	100	89	N	0.9	106	234	156	54	120	130	80	98	140	80	114	20	0	16	160	80	127	20	0	13	170	80	149	10	0	22	149	10.1	50	I
21	1164743	35	F	-	-	-	-	-	149	61	27.48	76	86	0.88	100	124	80	126	84	123	84	123	84	12.1	85	92	N	0.7	140	238	157	53	140	120	80	112	140	80	144	20	0	32	150	80	171	10	0	27	160	80	183	10	0	12	183	10.1	18	L
22	1220620	62	F	-	-	-	-	-	147	54	24.99	82	90	0.91	102	140	90	138	88	138	88	138	89	14.2	102	136	PR	0.4	146	225	155	33	187	140	80	102	160	80	119	20	0	17	170	90	136	10	0	17	170	90	163	0	0	27	163	10.1	68	H
23	1164736	59	M	+	+	+	+	+	162	92	35.06	86	96	0.9	96	140	90	136	88	138	88	137	88	16.4	101	170	PR	0.7	147	192	127	36	146	140	80	106	160	90	121	20	0	15	170	90	139	10	0	18	180	90	151	10	0	12	151	9.0	38	L
24	1220495	44	M	+	+	+	+	+	171	91	31.12	96	109	0.88	74	120	80	122	80	120	80	121	80	14.2	87	88	N	1.0	121	223	170	34	93	110	80	75	130	80	103	20	0	28	150	80	115	20	0	12	170	80	135	20	0	20	135	12.8	35	L
25	1238302	43	M	+	+	+	+	+	164	72	26.77	88	98	0.9	76	120	80	124	80	124	84	124	82	16.3	92	110	N	0.8	121	214	155	33	132	140	80	83	130	80	115	10	0	32	140	80	146	10	0	31	160	80	175	20	0	29	175	10.1	52	I
26	1163112	47	M	+	+	+	+	+	167	78	27.97	90	98	0.92	88	130	80	120	80	130	80	125	80	15.3	120	175	PR	0.8	125	201	122	43	178	130	80	87	150	80	137	20	0	50	160	80	153	10	0	16	160	80	169	10	0	16	169	10.3	39	L
27	1209978	49	M	+	+	+	+	+	168	70	24.8	82	100	0.82	84	130	90	128	84	124	86	126	85	16.1	294	343	D	0.8	110	187	97	37	267	130	88	87	130	90	112	0	2	25	150	90	130	20	0	18	160	90								

MASTER CHART

Sr. No.	O. P. No.	mograph		History				Anthropometry				General Physical Examination										Investigations																																				
		Age (Years)	Sex	DM	IHD	HTN	IHD	Smoking	Alcohol	Height (Cms)	Weight (Kgs)	BMI (Kg/m2)	Waist (Cms)	Hip (Cms)	WHR	BP reading (mm Hg)				Pulse Rate (/Min)	Hb (gm%)	Sugar			Lipid profile					Resting			Stage 1			Stage 2			Stage 3			Maximum HR (min)	CAD Probability score	Avg. CAD probability														
																1	2	3	Mean			FBS (mg/dL)	PPBS (mg/dL)	Diabetic status	Sr. Creatinine (mg/dL)	GFR (ml/min)	Cholesterol (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	TG (mg/dL)	SBP	DBP	HR (min)	SBP	DBP	HR (min)	Delta	SBP	DBP	HR (min)	Delta				SBP	DBP	HR (min)	Delta										
																																																	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
59	837660	52	M	-	-	-	-	168	81	28.7	96	110	0.87	90	140	90	138	88	134	88	136	88	15.7	101	88	PR	0.8	125	133	63	53	87	140	90	94	170	90	127	30	0	33	180	90	148	10	0	21	222	90	173	42	0	25	173	10.3	40	I	
60	1150120	47	M	-	-	-	-	173	73	24.39	83	99	0.84	90	132	80	130	80	126	78	128	79	13.8	88	94	N	0.9	124	184	115	38	155	130	80	93	140	80	123	10	0	30	160	80	148	20	0	25	180	80	171	20	0	23	171	10.2	54	H	
61	1150210	31	M	-	-	-	-	149	47	21.17	70	89	0.79	102	120	80	124	80	120	80	122	80	13.7	73	64	N	0.5	140	173	111	44	91	120	80	108	130	80	155	10	0	47	140	80	175	10	0	20	150	80	179	10	0	4	179	7.0	3	L	
62	1137501	42	M	-	-	-	-	160	54	21.09	82	102	0.8	72	120	80	124	80	126	80	125	80	15.0	100	67	N	0.9	130	130	76	39	73	120	80	71	150	80	113	30	0	42	160	80	141	10	0	28	170	80	142	10	0	1	142	10.4	30	L	
63	1137473	38	M	-	-	-	-	170	52	17.99	74	94	0.79	70	138	80	138	86	136	86	137	86	16.0	95	97	N	0.9	140	172	115	38	94	140	80	70	150	80	110	10	0	40	160	80	110	10	0	0	170	80	126	10	0	16	126	10.1	39	L	
64	1156546	39	F	-	-	-	-	O	162	75	28.58	86	100	0.86	80	136	80	138	84	138	84	138	84	16.0	86	88	N	0.9	116	200	124	39	184	140	80	79	150	80	115	10	0	36	160	80	127	10	0	12	170	80	142	10	0	15	142	11.7	29	L
65	1158726	43	M	-	-	-	-	162	70	26.67	76	96	0.79	96	130	80	128	80	130	80	129	80	14.5	119	128	D	0.8	126	204	153	34	87	130	80	109	140	80	138	10	0	29	150	80	160	10	0	22	160	80	175	10	0	15	175	10.1	52	I	
66	1158711	43	M	-	-	-	-	184	88	25.99	94	112	0.84	100	140	90	130	90	138	86	134	88	14.3	110	111	PR	0.8	124	134	36	52	228	140	90	98	140	100	118	0	10	20	150	100	139	10	0	21	170	100	150	20	0	11	150	10.1	60	H	
67	1158714	43	M	-	-	-	-	161	70	27.01	82	108	0.76	74	120	80	124	80	122	80	123	80	14.8	90	122	N	1.1	85	244	44	149	255	120	80	72	130	80	131	10	0	59	150	80	164	20	0	33	150	80	169	0	0	5	169	9.0	44	I	
68	1151740	30	M	-	-	-	-	168	71	25.16	83	98	0.85	90	130	80	130	80	130	80	130	80	12.7	86	88	N	0.8	132	222	147	39	179	120	80	100	130	80	133	10	0	33	140	80	169	10	0	36	150	80	184	10	0	15	184	10.1	41	I	
69	1138273	40	M	-	-	-	-	167	92	32.99	86	98	0.88	80	140	90	140	90	138	88	139	89	14.0	140	221	D	0.8	160	168	100	38	152	140	90	79	160	90	123	20	0	44	190	90	142	30	0	19	210	90	150	20	0	8	150	8.5	51	L	
70	1144756	28	F	-	-	-	-	152	48	20.78	60	83	0.72	70	120	80	124	80	122	80	123	80	14.9	79	90	N	0.6	125	145	95	38	62	120	80	70	130	80	105	10	0	35	140	80	126	10	0	21	150	80	137	10	0	11	137	9.4	13	L	
71	1136557	29	F	-	-	-	-	150	46	20.44	60	80	0.75	70	122	80	120	80	124	80	122	80	11.2	78	110	N	0.9	150	184	60	40	116	120	80	75	130	80	144	10	0	69	140	80	169	10	0	25	150	80	179	10	0	10	179	10.1	9	L	
72	997875	38	F	-	-	-	-	O	149	53	23.87	78	98	0.8	72	124	80	128	80	124	80	126	80	12.4	88	100	N	0.5	150	186	129	46	55	120	70	84	120	80	121	0	10	37	140	80	132	20	0	11	140	80	132	0	0	0	132	7.0	7	L
73	1009381	42	F	-	-	-	-	148	51	23.28	65	78	0.83	89	130	80	128	80	124	80	126	80	12.4	107	116	PR	0.8	148	223	164	84	126	130	80	73	130	80	127	0	0	54	150	80	146	20	0	19	156	80	150	6	0	4	150	7.2	47	I	
74	1008705	46	M	-	-	-	-	167	81	29.04	95	104	0.91	66	120	84	124	80	120	82	122	81	14.5	100	104	N	1.0	130	163	88	31	222	120	80	87	140	80	93	20	0	6	150	80	107	10	0	14	160	80	124	10	0	17	124	10.1	41	L	
75	1148475	53	M	-	-	-	-	163	62	23.34	82	108	0.76	94	130	80	120	84	124	84	122	84	14.7	139	143	D	0.9	124	165	105	36	119	120	90	108	140	90	138	20	0	30	150	90	156	10	0	18	180	90	186	30	0	30	186	10.1	44	I	
76	1136553	31	M	-	-	-	-	164	73	27.14	86	100	0.86	72	130	80	124	80	120	80	122	80	11.0	91	100	N	0.8	150	111	76	40	116	120	80	90	140	80	109	20	0	19	150	80	130	10	0	21	160	80	144	10	0	14	144	12.8	41	I	
77	997875	38	M	-	-	-	-	175	85	27.76	91	105	0.87	80	130	86	132	84	130	82	131	83	14.6	97	139	N	1.3	92	199	39	138	110	130	86	73	160	90	110	30	4	37	170	90	134	10	0	24	180	90	151	10	0	17	151	10.5	18	L	
78	721791	54	M	-	-	-	-	163	80	30.11	89	109	0.82	78	130	80	128	80	130	82	129	81	10.8	106	112	PR	0.8	120	164	93	36	174	130	80	67	150	90	125	20	0	58	160	90	151	10	0	26	170	90	169	10	0	18	169	9.0	49	I	
79	997873	41	M	-	-	-	-	O	170	75	25.95	86	101	0.85	74	140	86	138	88	136	86	137	87	15.8	104	136	PR	1.0	120	211	137	40	172	140	80	78	140	80	108	0	0	30	160	80	133	20	0	25	170	80	160	10	0	27	160	10.2	24	L
80	1150000	52	M	-	-	-	-	O	162	56	21.34	75	94	0.8	62	120	84	124	80	124	80	124	80	14.2	90	73	N	0.9	126	134	33	87	68	130	80	61	140	80	111	10	0	50	160	80	131	20	0	20	180	80	162	20	0	31	162	10.2	61	H
81	1151743	22	F	-	-	-	-	158	48	19.23	60	83	0.72	78	120	70	124	70	122	70	123	70	12.7	84	85	N	0.6	150	194	139	39	81	120	70	78	130	70	117	10	0	39	140	70	148	10	0	31	150	70	169	10	0	21	169	10.1	7	L	
82	1149233	59	M	-	-	-	-	163	46	17.31	64	84	0.76	96	130	80	124	80	130	80	127	80	11.6	114	109	PR	0.6	90	129	28	80	104	130	80	81	150	80	107	20	0	26	160	80	120	10	0	13	170	80	129	10	0	9	129	10.6	49	I	
83	1148490	58	M	-	-	-	-	161	62	23.92	65	87	0.75	70	120	80	124	80	120	80	122	80	13.9	97	94	N	0.7	130	168	104	39	124	120	80	66	140	80	110	20	0	44	140	80	131	0	0	21	160	80	171	10	0	20	151	10.5	59	I	
84	1150022	50	M	-	-	-	-	171	74	25.31	82	90	0.91	86	124	80	120	80	124	80	122	80	13.8	130	156	D	1.0	92	128	46	65	83	120	80	90	140	80	130	20	0	40	180	80	150	40	0	20	190	80	171	10	0	21	171	10.6	44	I	
85	1148476	53	M	-	-	-	-	163	62	23.34	82	106	0.77	102	130	80	132	80	128	80	130	80	14.7	139	143	D	0.9	140	165	105	36	119	120	90	108	140	90	138	20																			





### **ANNEXURE III**

#### **KEY TO MASTER CHART**

-	-	Absent
+	-	Present
B	-	Blunted
BMI	-	Body mass index
BP	-	Blood pressure
Creat	-	Creatinine
DBP	-	Diastolic blood pressure
dL	-	Decilitre
D	-	Diabetic
DM	-	Diabetes mellitus
F	-	Female
FBS	-	Fasting blood sugar
GFR	-	Glomerular filtration rate
gm	-	Gram
H	-	High
Hb	-	Haemoglobin
HDL	-	High density protein
HR	-	Heart rate
HRT	-	Heart rate recovery time
HTN	-	Hypertension
I	-	Intermediate

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IHD	-	Ischaemic heart disease
Kg	-	Kilogram
L	-	Low
LDL-C	-	Low density protein
m	-	Meter
M	-	Male
METS	-	Metabolic equivalents
mg	-	Milligram
Min	-	Minute
ml	-	Millimeter
mm Hg	-	Millimeter of mercury
N	-	Normal
O	-	Occasional
OP No.	-	Outpatient number
PPBS	-	Post prandial blood sugar
PR	-	Prediabetic
Pro	-	Probability
SBP	-	Systolic blood pressure
Sr	-	Serum
TG	-	Triglycerides
TMT	-	Treadmill test