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## Coexistence of Diabetes Mellitus and Hypertension - A Review

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### ABSTRACT

Diabetes mellitus and Hypertension are a common disease that is suffered by a huge percentage of total population. The coexistence of these two diseases is at a greater frequency than alone. Hypertension in the diabetic individual potently increases the risk and accelerates the risk of cardiac disease, stroke, peripheral vascular disease, nephropathy and retinopathy. The management of both this disease is equally important and the reduction in cholesterol level have significant role in preventing diabetic complication. Diabetic associated diseases like nephropathy also lead to the development of hypertension particularly in type I diabetic patient. The coexistence of hypertension in both type I and type II diabetic patients can lead to be increased peripheral vascular resistance and the exchangeable sodium ion can be a reason for hypertension in diabetics. The insulin resistance or hyperinsulinemia or elevated insulin can be one of the major pathogenesis of hypertension. In the present study we have reviewed the various literatures related to the coexistence of to life threatening disease that is hypertension and diabetic and it was observed that these two diseases are most commonly associated in a person. Thus there should be some modified treatment procedures for this kind of life threatening associated diseases.

**Keywords:** Diabetes Mellitus, Hypertension, Coexistence.

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## INTRODUCTION

Diabetes mellitus which is traditionally known as Madhumeha is not new to Indian traditional medicine. In Ayurveda already there is description about the sweetness of Diabetic urine which supports the treatment of diabetes with Ayurvedic traditional medicine. The word 'diabetes' (to flow through) was first used by the Greek physician in the 17<sup>th</sup> century. The sugar or sweetness existence in the urine of diabetes was established by Dobson in 1755<sup>1</sup>. According to the International Diabetes Federation (IDF) about 415 million people in the world have diabetes and about 78 million people of South-East Asia region is under diabetic condition. According to IDF by 2040 the total diabetic people population will rise upto 140 million. In the year 2015 about 69.1 million people of India have been reported as diabetic where this data was about 50.8 million in the year 2010<sup>2</sup>.

Hypertension or high blood pressure is a long term medical condition in which there is an elevation in the arterial blood pressure<sup>3</sup>. If the blood pressure goes above 140/90 it is considered as high blood pressure and it is said to be severe if the pressure is above 180/120. The high blood pressure is more deadly as it often has no visible symptoms. Thus if it is not treated, it can cause severe health problems such as stroke to mild heart disease, heart failure, coronary artery disease, effect in kidney also loss of vision is predominant<sup>4-6</sup>. As per the data of World Health Organization (WHO) the global burden of hypertension will be increased by 60% where 1.56 billion people will be affected by the end of 2025 in the various developed nation<sup>7</sup>. It was reported that about 25% of total death in 1990 was due to cardiovascular disease which is about 2.3 million individual. By the year 2020 it is predicted that there will be 111% increase in the total patient suffering from heart disease<sup>8,9</sup>.

For the modernized and industrialized civilization both the diabetes and hypertension has come the most common disease due to life style of the people. Out of the total population suffering from diabetes, half of them are hypertensive and about 5% and 25% of population with hypertension suffering from diabetes<sup>10</sup>. Thus the global burden for coexistence of diabetic and hypertension become the threat to world health care services<sup>11</sup>. In this study we have given emphasis to review the coexistence of diabetes and hypertension in individual and to know about the various study done regarding diagnosis, treatment, medication and prevention.

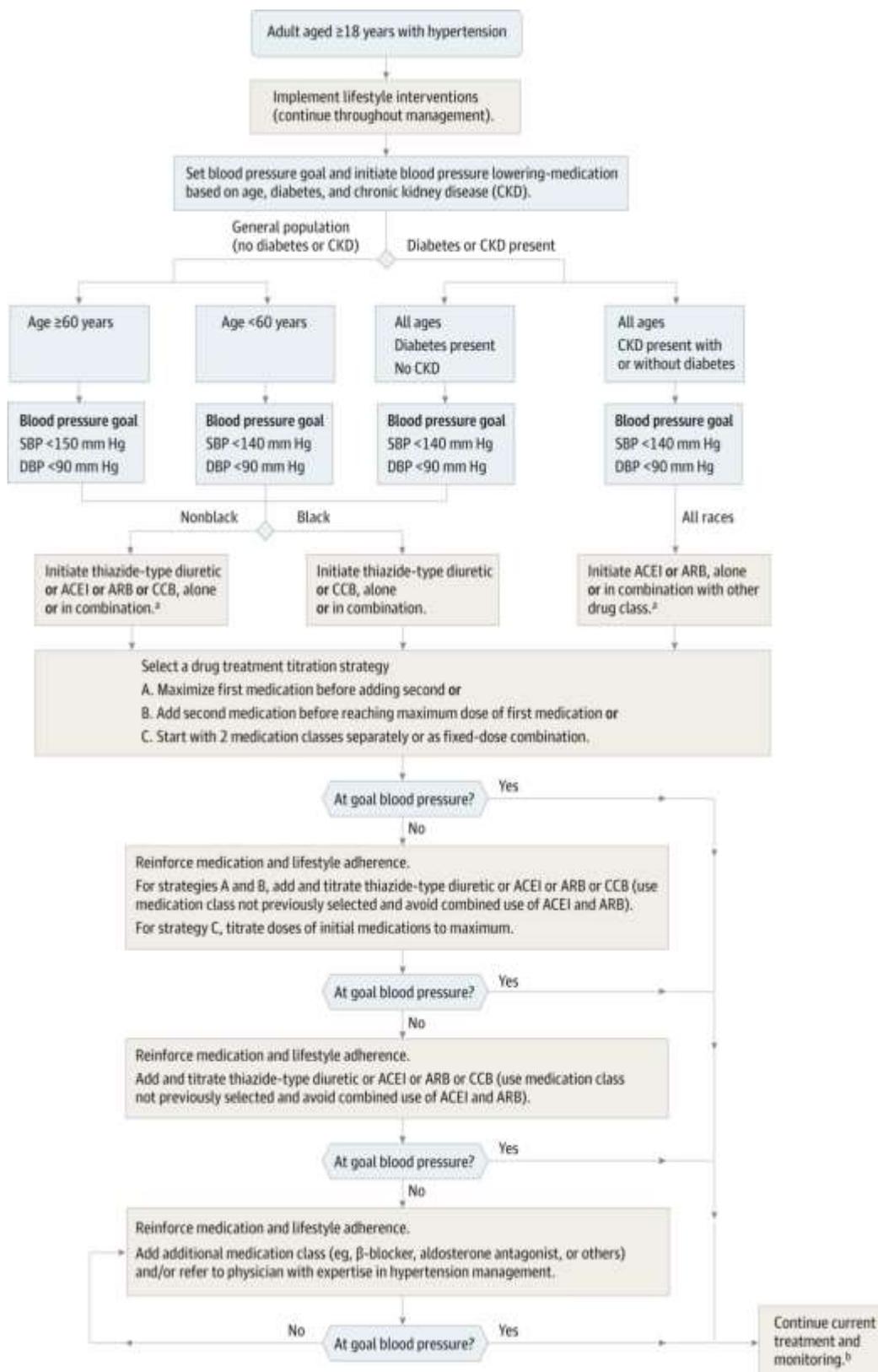
### **Existence of coexisting diabetes and hypertension:**

The patient who is a victim of coexistence of diabetes and hypertension (CDH) need to be taken ultimate care about his health as he is more prone to heart attack or stroke. A study reviles that

about 29% of the total patient suffering from CDH are unaware that they have high blood pressure too<sup>12</sup>. Study says that controlling of blood pressure acquires more important role on morbidity and mortality in CDH patient for diabetes than controlling blood glucose<sup>13</sup>.

Panda et al.<sup>14</sup> has carried out the study of prescription pattern of anti-hypertensive drug in hypertensive and diabetic hypertensive patient. In the study total of 422 prescriptions of 285 male and 137 female, were monitored in the age group of 35 to 75 years. Out of all 422 prescriptions, hypertensive patient was 118 and diabetic hypertensive patient was 304. In all the patient antihypertensive and antidiabetic drugs were used for the treatment specially the beta blocker or calcium channel blockers and biguanides or sulfonylurea respectively.

Mohan P. and Bhandare B.<sup>15</sup> have evaluated antihypertensive drug used in patients with coexisting type 2 diabetes mellitus with comparison to Eighth Joint National Committee guidelines in the outpatient department of General Medicine at Rajarajeswari Medical College and Hospital, Bangalore for 6 months (Aug 2014-Jan 2015). They have studied total of 150 cases for coexisting diabetes and hypertension. They have chosen age group of 55-70 years with male patient preponderance. Out of the total patient, 38.67% diabetic hypertensives patients were treated with monotherapy of anti-hypertensive drug and 61.33% of patients were treated polytherapy of anti-hypertensive drugs. They have concluded that the treatment of coexistence of hypertension with diabetes was in accordance with the Joint National Committee (JNC) 8<sup>th</sup> report (figure. 1).



**Figure 1: Panel members report of Eighth Joint National Committee (JNC 8): Evidence-Based Guideline for the Management of High Blood Pressure in Adults<sup>16</sup>.**

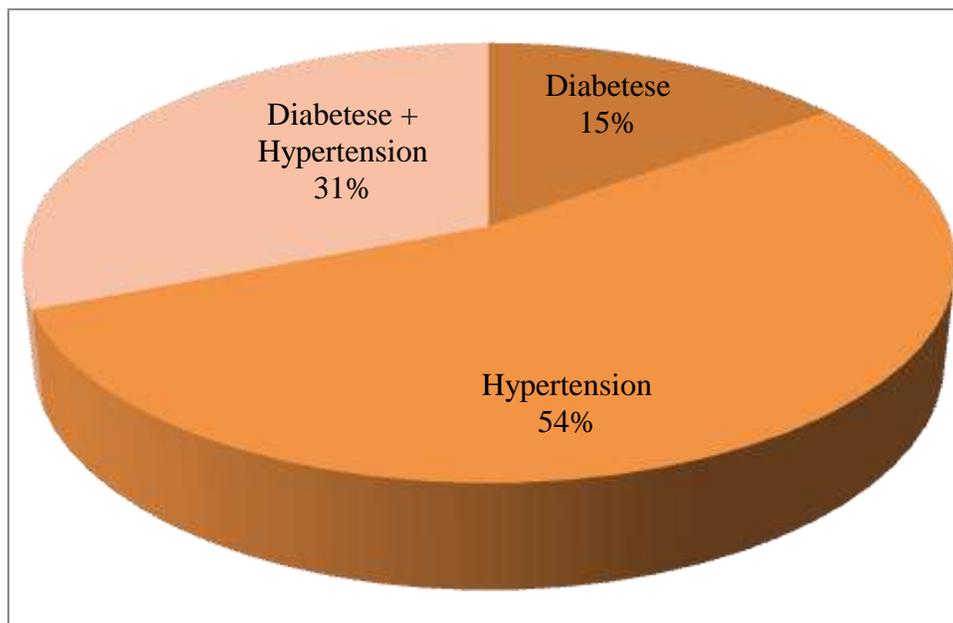
Legend:

*2014 Hypertension Guideline Management Algorithm SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; and CCB, calcium channel blocker. <sup>a</sup>ACEIs and ARBs should not be used in combination. <sup>b</sup>If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.*

Sweileh M. W. et al.<sup>3</sup> has investigated the consumption pattern of antidiabetic and antihypertensive medication among diabetic hypertensive patients. They have reviewed and analysed the prescriptions of 340 patients with type 2 diabetes mellitus and hypertension. They found that 74.3% was antidiabetic monotherapy and 47.3% was antihypertensive. They found the utilization of insulin combination therapy for the antidiabetic and other oral antidiabetic drugs. For the patient with hypertension combination therapy of low dose antihypertensive was utilized. They also reported with conclusion that there was an inappropriate uses of medications among the diabetic hypertensive patients which will increase the health and economical risk for the patient.

Rimoy G. et al.<sup>17</sup> has studied the management of hypertension in the three District Hospitals in Dares Salaam, Tanzania. They have studied 600 prescriptions where 2.2% was antihypertensive drugs. They found that 18.3%, 30.8% and 50.9% percentage of prescriptions contain both an antidiabetic and a thiazide diuretic in the 3 different hospitals respectively. In two of the hospital they have found that 54.8% and 45.2% of prescriptions were combination of drug containing an antidiabetic and propranolol. Also a combination of an antidiabetic, a thiazide diuretic and propranolol were found in 43.5%, 39.0% and 17.5% in the 3 hospital respectively.

Pandey V. et al.<sup>18</sup> has carried out the drug utilization studies (DUS) in outpatient department of Indian Institute of Technology Hospital, New Delhi, India. They have studied a total of 595 prescriptions of hypertensive and diabetic patients. Out of the 595 prescriptions 57.31% were males and 42.69% were females. They have found 54.62% of patients with hypertensive, 14.78% of patients with diabetic and 30.58% of patient with diabetic hypertension. 40.8% of antihypertensive patient utilized combination therapy and 52.96% of antidiabetic treatment was done by combination therapy.



**Figure 2: Percentage of patients having diabetes, hypertension and both diabetes and hypertension<sup>18</sup>.**

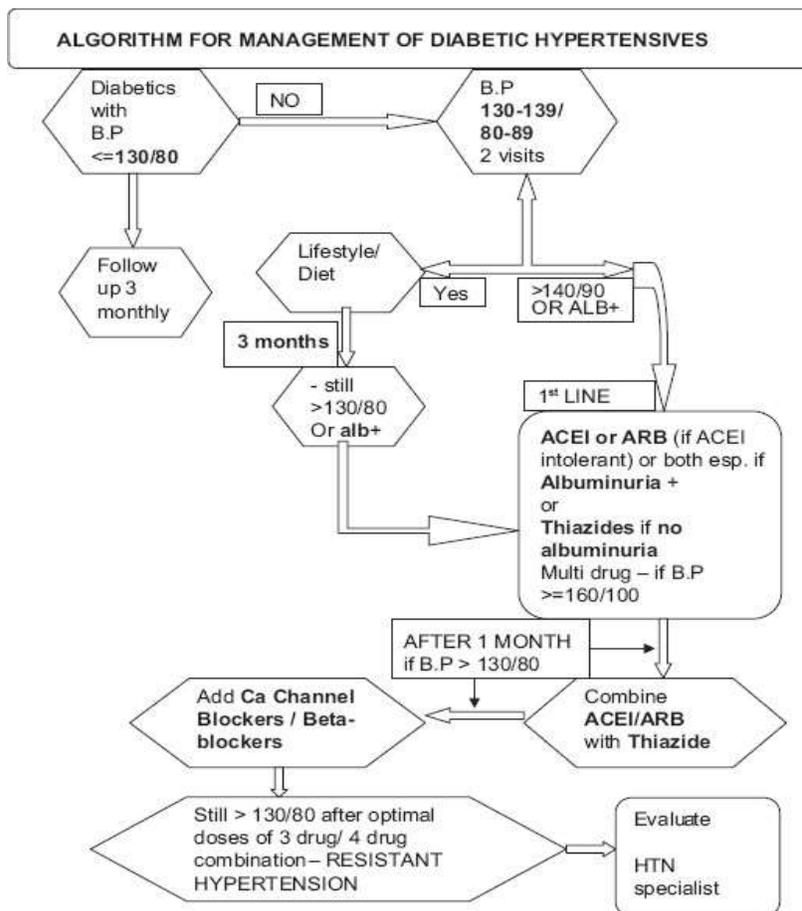
#### **Management of coexisting diabetes and hypertension:**

The management become very important as both the disease is the threat for the modernized society. The coexistence of diabetes and hypertension make the situation more complicated for the mortality and morbidity<sup>19, 20</sup>. This existence of both this diseases occurs in increasing frequency with increasing age. Study also reveals that, there is a common factor associated with both this disease, i.e. insulin resistance<sup>21</sup>.

A study reveals that 70% of patients with type II diabetes are having a blood pressure  $\geq 140/90$  mmHg which is mainly due to insulin resistance. This group of patients are more prone for other complications like premature microvascular and macrovascular diseases.<sup>22</sup> According to the United Kingdom Prospective Diabetes Study (UKPDS), every 10 mmHg decrease in mean systolic pressure was associated with reduced risk by 12% for any diabetic complication, 15% for diabetes-related deaths, 11% for myocardial infarction, 13% for macrovascular complications, and a no risk threshold was found for any end-point studies.

In the treatment of diabetic hypertension the controlling of blood pressure is more important. Thus in the coexisting diabetic hypertension the following condition has to be maintained:<sup>23-25</sup>

1. Goal (mmHg) for BP is  $<130 <80$  mmHg
2. Behavioural therapy alone (maximum 3 months), then add pharmacologic treatment if BP is 130–139/80–89 mmHg
3. Behavioural therapy + pharmacologic treatment if,  $\geq 140/\geq 90$  mmHg



**Figure 3: Algorithm for management of diabetic hypertension<sup>26</sup>.**

The hypertension and diabetes mellitus are coexist and are related to each other. If such condition is untreated it may leads for high risk to atherosclerotic cardiovascular disease. Changes in lifestyle and genetic history are causative for both the conditions. In the recent advancement of health care and study showed a greater interest in the clinical association between hypertension and diabetes.

#### **Guidelines for managing diabetic hypertension<sup>26-28</sup>:**

The various clinical trials done by organizations like American Diabetes Association (ADA), National Kidney Foundation (NKF) and Joint National Committee VII (JNC VII) and they have recommend a target blood pressure of 130/80 mmHg or less in hypertensive patient with diabetes.

- A. The target BP should be below 130/80 mm Hg.
- B. All routinely used antihypertensive drugs have been shown to be beneficial compared with placebo.
- C. More than one drug will usually be required to achieve the target BP.
- D. Patients with prehypertension (130-139/80-89 mmHg) should be given lifestyle/behavioural therapy alone for a maximum of 3 months and then, if targets are not achieved, should also be treated pharmacologically. Attention should be paid to

lifestyle changes (weight reduction; regular exercise; and moderation of sodium, protein, and alcohol), as well as control of hyperglycemia, dyslipidemia, and proteinuria, for all the patients.

- E. The choice of drugs should always include an ACE inhibitor (or an angiotensin II receptor blocker, if ACE inhibitors cannot be tolerated) and should usually include a diuretic. If additional therapy is needed, a calcium-channel blocker,  $\beta$ -blocker, or  $\alpha$ -blocker may be used.

The results of various studies suggested some aggressive approaches for the diagnosis and treatment of hypertension in reducing the prevalence of both diabetic macrovascular and microvascular complications. Study also gives strong evidence for the pharmacological treatment of hypertension in patients with diabetes which is effective in producing substantial reduction in complication of cardiovascular and microvascular diseases<sup>16, 29, 30</sup>. Patients who are having confirmed hypertension (systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg) should receive immediate pharmacological treatment in addition to lifestyle/behavioral therapy. According to JNC VII both therapies should be used simultaneously and immediately when there is a condition of systolic BP  $\geq 130$  mmHg or diastolic BP  $\geq 80$  mmHg. To achieve such condition usually a combination of 2 or more drugs or a modified drug delivery system is required.

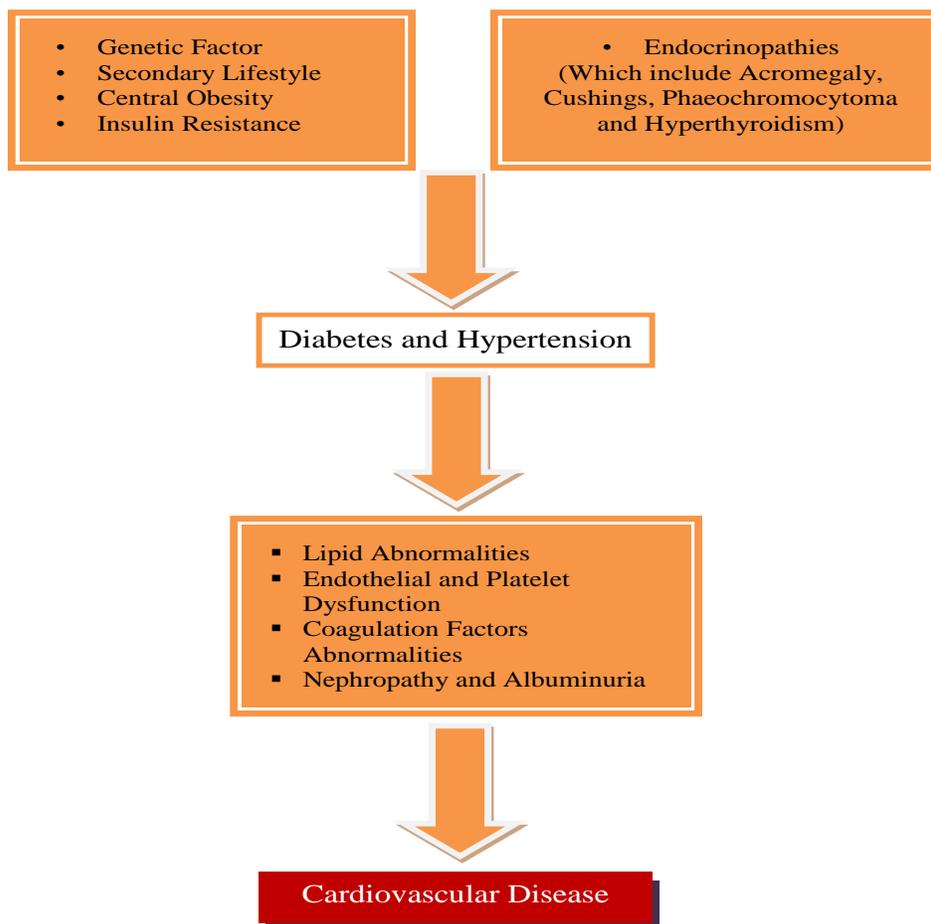
#### **Pathogenesis of Hypertension and the role of Hyperglycemia:**<sup>20, 31-35</sup>

The development of hypertension in diabetic individual due to hyperglycemia is caused by several mechanisms. The retention of Sodium and increase in exchangeable body sodium is one of the possible mechanisms for hypertension provoked by hyperglycemia. The increase in the glucose level in blood will increase the rate of glomerular filtration of glucose, which stimulate the tubular glucose-Na<sup>+</sup> co-transportation. These mechanisms is insulin independent and elevate the concentration of proximal tubular cell Na<sup>+</sup> and Na<sup>+</sup>, K<sup>+</sup>-ATPase activity in rat within 4 days when hyperglycemia is induced by streptozotocin. This cause the sodium retention during mild to moderate hyperglycemia and thus play the role to increase total exchangeable Na<sup>+</sup> with elevated blood pressure in patients with coexisting diabetes and hypertension.

In the patient with chronic hyperglycemia the vascular structure is changed and this may lead to vascular rigidity because at high concentration the glucose has direct toxic effect on endothelial cells. This effect may lead to decrease in endothelial vascular relaxation, increase constriction, hyperplasia of vascular smooth muscle and vascular remodelling.

The increase of glucose level in hyperglycaemia induces fibronectin and collagen-IV in human vascular endothelial cells. This enhanced in expression of fibronectin and collagen-IV thus may

further lead to endothelial dysfunction. Fibronectin which is a glycoprotein play a complex role in cell matrix interaction and thicken the glomerular basement membrane and magnesium with increase in expression. The hyperglycemia-induced local synthesis of fibronectin by endothelial cells may lead endothelial dysfunction as well as indirectly to increases in basement membrane production which yield in the hypertension. Furthermore, there is various evidence of having role hyperglycaemia in hypertension with complex mechanism.



**Figure 4: Pathogenesis of Cardiovascular Disease in diabetes and hypertension<sup>36</sup>**

#### CONCLUSION:

The increase globalization and modernization in life style of people has attributed many diseases. Cardiovascular and diabetes are the first line diseases which enhances the morbidity due to life style diseases. The group of patients who are suffering from hyperglycaemia are very likely to be more prone to have developed with hypertension. Both the disease alone itself causes the high risk of morbidity. The various literature surveys reveal that coexistence of both this disease is very common in the industrialized civilization era. The hypertension and diabetes mellitus are coexist and are related to each other. If such condition is untreated it may leads for high risk to

atherosclerotic cardiovascular disease. Changes in lifestyle and genetic history are causative for both the conditions. In the recent advancement of health care and study showed a greater interest in the clinical association between hypertension and diabetes. There is a necessity of an advance treatment for this coexistence of highly risk associated diseases.

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