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## **Interrelationship Between Diabetes Mellitus and Blood Pressure-(The Two Bad Twins)**

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### **Abstract:**

Diabetes Mellitus has rapidly become a major health threat in almost all the developing countries. This disease is said to be most commonly accompanied by Blood Pressure (Bad Companion/Buddy). These bad buddies together may lead to Cardiovascular Diseases and serve to be the cause for death and disability of a vast population. Before a decade, DM was a disease known to be prevalent in the age group above 40. Now a study (1) states that diabetes affects American Indians at a younger age more than any other ethnic population and is mostly type II diabetes mellitus. Blood pressure (BP) level is a major determinant of cardiovascular morbidity and mortality in individuals with diabetes mellitus. The Prevalence of type 2 diabetes is dramatically increasing dramatically worldwide (2) with the greatest rise in incidence occurring in adults under the age of 50, including young women.

The past 10 years have seen a troubling increase in the prevalence of DM2 in youth (3,4,5,6,7,). This epidemic of DM2 in youth has preferentially affected ethnic minorities (3,6). Using clamp studies, hypertension alone was found to associate with a decrease in glucose disposal by 27% (8). However, the combination of microalbuminuria and hypertension was associated with the greatest decrease in glucose disposal. In a research 84% of those with DM2 had elements of the insulin resistance syndrome-obesity, hypertension, dyslipidemia, or microalbuminuria (9). The insulin resistance syndrome may increase the risk for coronary artery disease and stroke by three times. This was stated in a Botnia Study. Thus from all the above mentioned studies, we can come to a conclusion that Diabetes is related to Blood Pressure.

### **Aim of this Review:**

The Purpose of this Review is to compile many existing studies on the Interrelationship between Blood Pressure and Diabetes. Thereby presenting how the Blood Pressure has an effect on the Diabetic patients and vice versa. This review also adds a note on the common disorders caused by the presence of both DM and BP.

### **Key Words:**

Diabetes, Hypertension, Related Disorders.

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### **Introduction:**

Arterial hypertension is clearly related to nephropathy in subjects with type 1 diabetes. In patients with type 2 diabetes insulin resistance seems to play a pivotal role in the pathogenesis of hypertension. (10). In the Hong Kong Cardiovascular Risk Factor Prevalence

Study, only 42% of people with diabetes had normal blood pressure and only 56% of people with hypertension had normal glucose tolerance [11]. In the US population, hypertension occurs in approximately 30% of patients with type 1 diabetes and in 50% to 80% of patients with type 2 diabetes [12]. A prospective cohort study in the United States reported that type 2 diabetes mellitus was almost 2.5 times as likely to develop in subjects with hypertension as in subjects with normal blood pressure [13]. In reality, diabetes and hypertension are found in the same individual more often than would occur by chance, whereas the overlap between dysglycemia and raised blood pressure is even more substantial than that between diabetes and hypertension [14]. In accordance with the Third National Health and Nutrition Examination Survey, 1988-1991, it has been reported that [15], Twenty-four percent, or an estimated 43 million, of the adult, civilian, noninstitutionalized population of the United States had hypertension. The overall prevalence of hypertension was slightly higher among men than women. Thus one cannot be treated without controlling the other. This review Provides a better understanding of the relationship between DM and BP thus aiding in the early diagnosis and treatment of Diabetes and hypertension.

### **Prevalence of Diabetes:**

Type 2 diabetes is on the verge of becoming a pandemic in India.[16]. As type 2 diabetes shares several risk factors in common with coronary artery disease (CAD), such as age, hypertension, dyslipidemia, obesity, physical inactivity, and stress, an increase in the prevalence of diabetes indirectly implicates an escalating risk of CAD as well.[17,18]

There are currently 135 million people with diabetes in the world, and India leads the world with 40.9 million people in diabetes in 2007.[19]. Moreover, it is projected that, by the year 2025, 80.9 million will have diabetes in India. The prevalence of diabetes in urban Indians has steadily increased from 2.1% in the 1970s[20] to 8.2% in the 1980s,[21] later climbing to 12–16%.[22,23]

Thus the phenomenon of high prevalence of diabetes reported among migrant Asian Indians[24] has now spread to urban India and is rapidly moving to rural areas as well.[25]. There is still inadequate population-based data on the prevalence of CAD in India, particularly comparing diabetic and nondiabetic subjects.D9

### **Prevalence of Hypertension:**

Hypertension is a highly prevalent disease worldwide and very common among the patients with diabetes. The prevalence of hypertension in diabetic patients is approximately twice that of the non diabetic population<sup>1</sup>. The incidence of diabetes mellitus is rapidly rising and will soon affect 300 million people worldwide while more than half of them will be hypertensives.[26]

In the past two decades according to the U.S. Renal Data System[27], there has been continual increase in the incidence of end-stage renal disease among patients with diabetes, predominantly of those with type 2 diabetes.

Recent reports from the United States have shown that almost two thirds of adult diabetic population use antihypertensive therapy or have blood pressure >130/80 mm Hg,[28]

### **Hypertension Following Diabetes:**

In recent decades several clinical trials are investigated the effect of treatment of diabetes on CV risk reduction in both type I and type II diabetes mellitus. This is also presents conflicting results [29-32] in United Kingdom prospective diabetes study in newly diagnosed T2D patients. The early intensive treatment of diabetes within the first 5 years of commencement resulted in long term reduction of CV disorders [29]

In the veterans affairs diabetes trials (vadt) [30], older patients with the 10 years mean duration of diabetes had no cardio vascular benefit when submitted to an intensive glycemic controlled regiment. This population has 40% of patients with previous history of cardio vascular disease.

In T1D patients the diabetes controlled and complications trial / epidemiology of diabetes interventions and complications study showed the cardio vascular benefits of an intensive glycemic control after a follow up of 17 years [33]. This early protection is postulated as metabolic memory which means that the effect of early glycemic exposure resulted in protective effects. [34].

Approximately from 10-30% of T1D and 60% of T2D have hypertension [35-36]. The co-existence of these 2 condition increase the risk of developing macro vascular complications like myocardial infarction and stroke and also microvascular complications like nephropathy and retinopathy. [37]. The recommended target blood pressure for patients with diabetes according to ADA [38] is characterized by BP < 130 or 80mmHg [39].

### **Common Disorders associated with Diabetes and Hypertension:**

there are some common metabolic disorders associated with both the diabetes (T2D) and hypertension. These diseases are of prime importance in evaluating the net combining effects of diabetes and hypertension. Some of the most important disorders are discussed here under.

### **Insulin Resistant Syndrome:**

These would include cell membrane ion exchange, enhanced sympathetic and renin-angiotensin-aldosterone system activity (RAAS) as well as suppressed atrial natriuretic peptide activity, sodium retention with consequent volume expansion, progressive renal disease, cardiac hyperactivity, left ventricular hypertrophy, dyslipidemia, chronic hyperglycemia and increased oxidative stress.[40]

In untreated patients with essential hypertension, fasting and postprandial insulin levels are higher than in normotensive controls, regardless of the body mass index, with a direct correlation between plasma insulin concentrations and blood pressure level[41]. A genetic predisposition to insulin resistance and hypertension is present in patients with type 2 diabetes mellitus[42]

studies have shown that arterial hypertension and type 2 diabetes appear to be associated clinically as a syndrome involving also other conditions such as dyslipidemia, central obesity, hyperuricemia and accelerated atherosclerosis.[43-44]. This syndrome has been described as insulin resistance syndrome[45], metabolic syndrome[44]or "syndrome X".[46].

### **Hyperglycemia:**

Hyperglycemia is a strong risk factor for the occurrence and progression of microalbuminuria, but has a lesser impact on progression at more advanced stages of kidney disease, at which hypertension, hypercholesterolemia, and genetic factors play a greater role in shaping the outcome. In Pima Indians, 2-hour plasma glucose concentration, fasting plasma glucose concentration, and hemoglobin A<sub>1c</sub> each predict elevated albuminuria, defined as an ACR  $\geq 30$  mg/g, after adjusting for age, sex, and duration of diabetes [47].

### **Diabetic Nephropathy:**

A family history of hypertension increases the risk for developing DN. In Pima Indians with type 2 diabetes, the prevalence of proteinuria was similar if neither parent or only one parent had hypertension (8.9% and 9.4%, respectively), but was significantly higher if both parents had hypertension (18.8%). When both parents had hypertension, the odds for proteinuria in the offspring were two times that if only one parent had hypertension. This association remained even when controlled for age, sex, duration of diabetes, 2-hour postload plasma glucose concentration, mean arterial pressure, and its treatment in the offspring and for diabetes in the parents [48]. In addition, higher blood pressure before the onset of type 2 diabetes is related to a higher prevalence of elevated albuminuria after the onset of diabetes, suggesting that blood pressure plays a causal role in DN development [49].

### **Obesity:**

Obesity is a major risk factor for diabetes, hypertension, and CVD, which in turn increase the risk for DN. The increasing prevalence of obesity in Pima Indian youth combined with a nearly fourfold increase in the frequency of exposure to diabetes in-vitro has shifted the onset of diabetes to younger ages [50]. Even though the proportion of youth developing diabetes among the Pima Indians and in the general US population is small, the current epidemic of obesity in this age group is already associated with an increasing incidence of diabetes in childhood and adolescence [51].

## **Inflammation and Oxidative Stress:**

A low-grade inflammatory process occurs in both diabetes and hypertension [52-56]. Even chronic periodontitis is a latent factor in the development of diabetes, hypertension, cardiovascular diseases, and the metabolic syndrome [57-63]. In some ways, diabetes and hypertension could be considered as chronic inflammatory diseases.

Inflammatory markers (eg, C-reactive protein (CRP)) are increased in patients with diabetes, hypertension, and the metabolic syndrome, and also predict the development of these diseases [64-66]. The local renin-angiotensin-aldosterone system (RAAS) plays a very important role in vascular pathophysiology. Angiotensin-converting enzyme (ACE) is expressed in the shoulder of coronary artery plaques. Angiotensin II (Ang II) is to a large degree responsible for triggering vascular inflammation and inducing oxidative stress [67]. It stimulates NADH/NADPH oxidase, and activates Rho/Rho kinase, protein kinase C (PKC), and mitogen-activated protein kinase (MAPK) [71]. Also, Ang II down-regulates proinflammatory transcription factors such as nuclear factor- $\kappa$ B (NF- $\kappa$ B), resulting in the generation and secretion of reactive oxygen species (ROS), inflammatory cytokines (eg, interleukin-6 [IL-6]), chemokines, and adhesion molecules [72,73].

## **What could be done?**

Dietary modification, regular physical activity, weight reduction, and cessation of smoking have been proven to be beneficial in preventing CAD. The Harvard Alumni Study documented that physical inactivity plays a role in CAD.[74] Though there are very few studies on the role of exercise in prevention of Hypertension in diabetes patients, there is ample evidence to support that exercise does reduce cardiovascular risk factors and thus can potentially be of great help in reducing CAD itself.[75-78]

**Exercise training:** Exercise training improves exercise capacity and quality of life in patients with mild to moderate heart failure. Early trials have shown beneficial effects of aerobic exercises. More recent trials show that an element of resistance training improves muscle strength, bulk and endurance.[79,80]. A low level to a moderate intensity (50-80% of maximal capacity) exercise with a warm up period of period of 10 to 15 min, for a duration of 20 to 30 min, 3-5 times a week is recommended in heart failure patients[81].

**Diet and nutrition:** Heart failure patients are at increased risk of weight loss due to loss of appetite and hypercatabolic status. Adequate calorie intake and nutrients are part of the dietary programmes in these patients. Salt restriction according to symptoms is an essential component. Fluid balance has to be maintained. A supervised nutritional intervention was shown to improve clinical status and quality of life in heart failure patients.[82].

## **Conclusion:**

This Review presents the the Interrelationship between diabetes and Blood Pressure and also the common disorders which they form etiology for. Diabetes and hypertension share common pathways such as SNS, RAAS, oxidative stress, adipokines, insulin resistance, and PPARs

.These pathways interact and influence each other and may even cause a vicious cycle. Hypertension and diabetes are both end results of the metabolic syndrome. They may, therefore, develop one after the other in the same individual. Central obesity is the cause of the metabolic syndrome. [83]. Its is necessary to understand their common pathway for providing high treatment possibilities. Therefore, optimization of lifestyle remains the cornerstone in the prevention and treatment of diabetes and hypertension.

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