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Diabetes and Hypertension - A Challenging Alliance

M Maksumul Haq[1]

Hypertension has created a havoc worldwide. According to World health statistics released in 2012 (collective data of 194 countries), one in three people has hypertension and one in ten has diabetes, causing a dramatic increase in heart disease and other chronic illnesses, particularly in low- and middle-income countries. Bangladesh is going through a transition phase where death rate from communicable diseases (CD) are declining and non-communicable diseases (NCD) like Type 2 Diabetes (T2DM) and essential hypertension (HTN) are increasing. A report from International Center for Diarrhoeal Diseases in Bangladesh (icddr,b) mentioned that there is a massive shift from CDs to NCDs and mortality due to cardiovascular and cerebrovascular diseases has increased by a massive 35 times from 1986 to 2006.[1]

Prevalence of T2DM and HTN varies from country to country and is showing an increasing trend. It is projected that the total number of people with T2DM will rise from 171 million in 2000 to 366 million by 2030. The number of adults with HTN in the world is predicted to increase by 60% to a total of 1.56 billion people by 2025.[2] A meta analysis done in icddr,b showed pooled HTN prevalence in Bangladesh within each 5 year time period was: 11% in 1995-2000, 12.8% in 2001-2005, and 15.3% in 2006-2010.[3] The same study showed prevalence of T2DM 3.8%, 5.3% and 9% respectively during the same time frame.

The frequency of these diseases increases with increasing age. The burden of this disease is not only increasing by the number of people affected but also by the fact that it is occurring at younger age. The registry of Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine, and Metabolic Disorders (BIRDEM) reveals that the mean age at diagnosis of T2DM was significantly lower in 2005 compared to that in 1995.[4]

T2DM and HTN are frequently clustered together. The coexistence of these two diseases at a greater frequency is not due to chance alone. The frequency of association of these two diseases is between 20-60% depending on age, obesity and ethnicity. In T2DM, hypertension is commonly associated with part of metabolic syndrome and many of the patients have resistant hypertension. On the other hand in type 1 diabetes, hypertension develops with the onset of renal disease which is usually after 15 years. The development of renal disease in diabetes definitely contributes to the development of HTN, although mostly remains "essential".

Our understanding for this common association is multi-factorial and also incomplete. Essentially all patients with T2DM are insulin resistant, whereas about 50% of those with essential hypertension are insulin resistant.[5] T2DM develops when compensatory hyperinsulinemia cannot cope with hyperglycemia and HTN develops when insulin acts on insulin-sensitive tissues other than β-cells. T2DM is associated with insulin resistance along with stimulation of sympathetic nervous system and the renin-angiotensin system leading to hypertension. Diabetes is associated with proliferation of vascular smooth muscle cells leading to hypertension. Abdominal obesity and visceral omentum are also related to both these diseases. Omentum may act as the common soil which leads to the development of these diseases as adipokines including angiotensinogen is secreted in large amount from this tissue.

Authors' Information:

1. ***Professor M Maksumul Haq,*** *MBBS, FCPS, FRCP, FACC, Senior Consultant & HoD, Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka-1000.*

The target organs affected by these two diseases are vascular tree and hypertension accelerates the complications of diabetes. In observational studies, people with both diabetes and hypertension have approximately twice the risk of cardiovascular disease as hypertensive without diabetes. Combination of diabetes and hypertension not only increases the risk of macrovascular complications like coronary artery disease and cerebrovascular disease (TIA, stroke etc.) but also microvascular disease like nephropathy (micro-albuminuria, macro - albuminuria, renal failure etc.), retinopathy and neuropathy (foot ulcer, gangrene sexual dysfunction etc.). One-third to three-quarters (35-75%) of diabetic complications are attributable to hypertension.[6] Coexistence of HTN and diabetes can pose additional risk in some subsets of patients. Pregnancy with diabetes and hypertension carries increased risk of pre-eclampsia. Children with type 1 diabetes and hypertension are particularly vulnerable to end-organ disease because of early exposure to cardiovascular risk factors.[7]

The risk of coronary events in diabetes is two-fold in men and four-fold in women. This increase is even seen in premenopausal periods. The part of this increase is due to associated risk factors like hypertension, dyslipidaemia and clotting abnormalities. United Kingdom Prospective Diabetes Study (UKPDS)[8] has shown that each 10-mmHg decrease in mean systolic blood pressure was associated with reductions in risk of 12% for any complications related to diabetes, 15% for deaths related to diabetes, 11% for myocardial infarction, and 13% for microvascular complications. No threshold of risk was observed for any end point.

The target blood pressure in diabetic hypertensive is less than 130/80 mmHg. This target was based on two trials HOT[9] and UKPDS.[10] However after ACCORD-BP trial the validity of this specific goal remains a subject of debate and research.[11] ACCORD-BP trial compared systolic BP goal of lower than 140 mmHg vs. lower than 120 mmHg but found no difference in the primary outcome which were a composite cardiovascular death, nonfatal myocardial infarction and nonfatal stroke. The target to treat is to slow the progression of target organ damage, or ideally to prevent it entirely. Renin-Angiotensin-Aldosterone System (RAAS) blockade by angiotensin-converting enzyme inhibitors and angiotensin receptor blockers has been reported to be best for this group of patients. However in most of the cases additional antihypertensive drugs are required in which case a calcium channel blocker or thiazide like diuretic is preferred. Beta-blockers have been reported to adversely affect the overall risk factor profile in the diabetic patient. Aggressive control of blood pressure, glucose levels and lipids should be attempted to reduce the cardiovascular risk of diabetic hypertensive patients. However recent reports of aggressive control of both blood pressure and glucose are not encouraged especially in elderly populations. Low dose aspirin therapy as a primary preventive strategy in diabetic hypertensive patients introduced after HOT trial is recently challenged by other trials[12] and the role of low dose aspirin remains unclear.

The association of HTN and T2DM has been recognized for many years but we now understand the additional facets of the problem such as dyslipidaemia, obesity, hypercoagulability and chronic kidney disease which all needs to be addressed during their management. Combination of diabetes and hypertension is a significant economic burden on health care. Early detection and appropriate management is of paramount importance for preventing or delaying the progression of target organ damage.

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