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Domination of Nephrotic Problems among Diabetic Patients of Bangladesh

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Abstract

Nearly 80% of people with diabetes live in low and middle-income countries. It increases healthcare use and expenditure and imposes a huge economic burden on the healthcare systems. The International Diabetes Federation estimated 7.1 million people with diabetes in Bangladesh and almost an equal number with undetected diabetes. This number is estimated to double by 2025. It is a costly condition and can lead to stroke, heart attack, chronic kidney diseases, neuropathy, visual impairment and amputations. Bangladesh is a developing country where 75% of total population lives in rural area. Subsequently they have poor healthcare access as 26% of rural professionals remain vacant and nearly 40%, absent. Nearly 45% rural people take medical assessment from unqualified health workers including medical assistants, mid-wives, village doctors, community health workers in comparison to that by qualified medical graduates (only 10%-20%). More than 75% women having complications sought treatment from an unqualified provider. These are mostly because concern over medical costs, and pronounced socioeconomic disparities found for care-seeking behaviour in both urban and rural Bangladesh.

Keywords: Diabetic patient; Diabetic kidney disease (DKD); End stage renal disease (ESRD); Diabetic nephropathy (DN); Chronic kidney disease (CKD); Diabetes mellitus (DM)

Introduction

During 90's, the country has a relatively low diabetes affected population. According to the International Diabetes Federation, the prevalence will be around 15% by 2030. With diabetes, the small blood vessels in the body are injured. When the blood vessels in the kidneys are injured, they cannot filter blood properly. About 30% of patients with Type 1 (juvenile onset) diabetes and 10%-40% of those with Type 2 (adult onset) diabetes eventually will suffer from kidney failure. The earliest sign of diabetic kidney disease is an increased excretion of albumin in the urine. This happens long before the usual tests done after seeing a physician. Diabetic kidney disease (DKD) is a progressive condition and is an important cause of end stage renal disease (ESRD) as well as a risk factor for cardiovascular morbidity and mortality. There is general agreement that people with diabetes should be screened regularly to detect early markers of kidney damage. People with diabetes and micro-albuminuria should be treated with a multifactorial intervention approach to retard the progression of DKD.

Materials and Methods

A comprehensive review of literature search including books, journal, newsletters, newspaper, magazine column and many more; some physicians, technical experts,

industry high officials, hospital authority, nurses and employees of pharmacy companies stated their valuable observation. Projections were based on nephrotic disorders prevalent in diabetic patients, their treatment and statistical evaluation in several institutions of Bangladesh.

Results and Discussion

General pathophysiology and prevalence of diabetes complications

Chronic kidney disease (CKD) was defined in terms of kidney damage (albuminuria) and decreased kidney function (decreased estimated glomerular filtration rate (eGFR)) [1]. Albuminuria was defined as an albumin-to-creatinine ratio greater than 2.5 mg/mmol or 3.5 mg/mmol for men and women, respectively, on at least two occasions [2]. Type 2 diabetes mellitus (DM2) globally affects 18%-20% of adults over the age of 65 y. Diabetic kidney disease (DKD) is one of the most frequent and dangerous complications of DM2, affecting about one-third of the patients with DM2 [3]. The conventional treatments for DKD are control of blood glucose and blood pressure levels by inhibiting the renin-angiotensin system. However, the prevalence of DKD continues to increase and additional therapies are required to prevent or ameliorate the condition. Many drugs have been, or are being, developed to target the molecular mechanisms in play in DKD [4]. Diabetic nephropathy is the commonest cause of end-stage renal disease (ESRD) in the USA. End-stage renal disease (ESRD) incidence due to type-2 diabetic nephropathy (DN) is 35%-50%, according to the United States Renal Data System [5]. The next most common cause is hypertension [6]. The third most common cause is glomerulionephritis. The important subgroups of glomerulonephritis include: immunoglobulin A nephritis (IgA), membraneous glomerulonephritis (MGN) and focal sclerosing glomerulonephritis (FSGN). Among all the complications of diabetes mellitus, nephropathy is the diabetes-specific complication with the greatest mortality [7]. Recently, there appears to have been an explosion in the incidence of diabetic nephropathy (DN), which is most often type II, or non-insulin dependent diabetes mellitus (NIDDM). The increased incidence of NIDDM appears linked to a virtual epidemic of obesity in the USA [8].

Prevalence of diabetes in Bangladesh

An estimated 10 million people in Bangladesh have diabetes [9]. WHO stated 83% population of age group 25-65 y never checks for diabetes [10]. A different report says almost similar thing. For an effective control and prevention of diabetes; 87% of Bangladeshis were non-compliant, compared to 71% of Indians and 52% Europeans [11]. Interesting thing is compliance is not improved in the last 14 y. 33% people age over 35 y are diabetic or pre-diabetic, only 12% of them have their condition under control [12]. According to the WHO-diabetes country profile of Bangladesh in 2016, the physical inactivity was prevailing among 25.1% of population [13].

Diabetes patients in Bangladesh with renal dysfunction

Glomerulonephritis was found to be the leading cause of end stage renal disease (ESRD) and diabetic nephropathy was the second common cause. Hypertension was the most common associated comorbid disease [14]. As kidney function deteriorates, patients develop complications related to fluid overload, electrolyte and acid-base imbalances, and the build-up of nitrogenous waste products. To survive, some patients eventually need haemodialysis or kidney transplantation [15]. 40%-50% of patients with type 1 diabetes and 20%-30% of patients with type 2 diabetes developed diabetic nephropathy [16]. In BIRDEM 2014, prevalence of nephropathy was found in 25% patients; male 27% and female 22% found among 400 type-2 diabetic patients [17]. +35A>C polymorphism possibly responsible for nephropathy in Bangladeshi type-2 diabetic subjects which is predominant in male [18]; Micro-albuminuria was found in 24% of type 1 diabetes, 27% of fibrocalculous pancreatic diabetes, and nearly 70% of type 2 diabetes children and adolescent in Changing Diabetes in Children (CDiC) clinic, BIRDEM [19]. In Bangladesh, the causes of CKD G5 among 954 patients who were on HD in 2012-2013 were chronic glomerulonephritis (25.5%), diabetic nephropathy (41%) and hypertensive renal disease (33%) [20].

Non-adherence to preventive and therapeutic lifestyle

Diabetic Association of Bangladesh selected 374 type 2 diabetic patients diagnosed for at least one year. Non-adherence rate of diet was 90% and exercise was 25%. About 32% patients non-adhered to self-blood glucose monitoring, 70% to foot care and 6% had smoking habits. The main barriers to adherence to blood glucose monitoring was that they did not believe it is useful (65%) and barriers to do exercise were always being busy (44%) and coexisting diseases (9%) [21].

Diabetic forecast

Almost one in ten adults in Bangladesh was found to have diabetes, which has recently become a major public health issue. A recent meta-analysis showed that the prevalence of diabetes among adults had increased substantially, from 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010. International Diabetes Federation stated

the prevalence will be 13% by 2030 [22]. According to the WHO, at least 2.8% of the population worldwide suffer from diabetes. Considering the increasing rate of type 2 diabetes it is understood that, by the 2030 the prevalence of diabetes mellitus will be double [23].

Healthcare expenditure for diabetes in Bangladesh

A recent study by World Bank found $160 per year in household expenses for diabetes care (2013 dollars) in Bangladesh [24]. The annual cost of diabetes care per person in the outpatient department of a tertiary care facility was $314. Based on this finding, it is estimated that the total annual burden of some 5.1 million diabetic patients will be $1.5 billion, which is a large burden for a developing country like Bangladesh [25]. In 2016, approximately 55,703 diabetic individuals received in-hospital care, with an estimated 2,641,000 outpatient visits. The total annual estimated cost of diagnosed diabetes was approximately $217.71 million [26]. The median monthly cost of diabetes maintenance was close to USD 10, approximately 10% of the median monthly income [27].

Management of nephrotic complication in diabetic patients

Blood pressure control: Blood pressure is one of the most important factors influencing progression of diabetic kidney disease and therefore should be aggressively controlled. The SPRINT trial showed reduced mortality in people with non-diabetic CKD with lower blood pressure targets (<120/80). In patients with diabetes or kidney disease, KDIGO recommends treating patients to a blood pressure of <140/90 in absence of proteinuria and <130/80 mm Hg in presence of proteinuria. The first-line agents for treatment of hypertension in people with diabetes are ACE-Inhibitors (type 1 diabetes) or Angiotensin Receptor Antagonists (ARB) (type 1 or 2 diabetes) [28,29].

Using multiple agents/combination therapy: The majority of hypertensive patients with diabetes require more than one agent to control blood pressure to the recommended target level; Diuretics or/and calcium channel blockers may be added to ACE-Inhibitors or angiotensin receptor antagonists. Thiazide diuretics, such as chlorthalidone, are similarly effective in reducing coronary heart disease. However, their use in diabetes is less optimal given their metabolic adverse effects, such as hyperglycemia [30].

Inhibition of the renin-angiotensin system: The RAAS plays a central role in the pathogenesis and progression of diabetic kidney disease. Therefore, inhibition of this system with ACE-Inhibitors or ARBs is one of the most important steps in the treatment of DKD. All hypertensive patients with diabetes should be treated with an ACE-Inhibitor or ARB. Normotensive patients with micro-albuminuria or macro-albuminuria may benefit from treatment with an ACE-Inhibitors or angiotensin receptor antagonists. From a kidney perspective there is no data to support treatment of normotensive, normo-albuminuric patients with ACE-I or ARBs, although there may be some benefit for retinopathy. Patients who are intolerant to ACE inhibitors due to cough usually tolerate an ARB. While angioedema has also been reported with ARBs, it is a rarely seen side effect and much less common that with ACE-Inhibitors. Aldosterone antagonists (spironolactone, epleronone) and direct renin inhibitors (aliskerin) reduce proteinuria in short-term studies but have not been demonstrated to prevent the development or progression of DKD or cardiovascular disease [31,32].

Blood glucose control: It plays an important role in the prevention and progression of DKD and other microvascular diabetes complications. Therefore, good glycemic control is critical for the management of kidney disease and other diabetic complications in these patients. In general, the ADA recommends an HbA1C goal of <7%. However, many patients with CKD are at increased risk of hypoglycemia, particularly the older patients with much co-morbidity, and should be considered for higher glycemic targets [33].

HbA1c in DKD: Chronic kidney disease, end stage kidney disease (ESRD) and treatment with erythropoiesis stimulating agents (ESAs) have been shown to be associated with decreased red blood cell survival or an increase in red blood cell production/turnover, thereby causing artificially low HbA1C levels in some of these patients. Other reports have shown an increase of HbA1C in CKD through possibly carbamylation of haemoglobin or acidosis. As a result HbA1C levels may not be as accurate in assessing glycemic control in patients with CKD or ESRD. Effects of DKD on glucose control. With advanced GFR loss, typically<20 mL/min/1.73 m2 or ESRD, insulin catabolism is diminished and gluconeogenic capacity by the kidney is impaired. Therefore glucose-lowering therapy often requires reduction to avoid hypoglycemia [34].

Sodium-glucose co-transporter 2 (SGLT2) Inhibitors for type 2 DM: SGLT2 inhibitors have emerged as a novel class of medications for the treatment of type 2 DM and have been demonstrated to have beneficial effects beyond their glucose lowering abilities both for cardiovascular and renal endpoints. Empagliflozin has been demonstrated to reduce worsening DKD (defined as progression to macro-albuminuria, doubling of serum creatinine or initiation of renal replacement therapy). The mechanism for this is thought to relate to renovascular effects of the medication. Canagliflozin has been found to

reduce the incidence of worsening albuminuria, reduction in GFR and need for renal replacement therapy. SGLT2 inhibitors are, however, not indicated for patients with reduced GFR (eGFR<60 ml/min for Dapagliflozin and eGFR<45/min for Canagliflozin and Empagliflozin) [35-37].

Statins and diet modification: Hyperlipidemia is common in diabetic patients with renal disease. Treatment with a statin does not affect progression of kidney disease, but reduces cardiovascular disease risk in people with diabetes and chronic kidney disease. Therapy with a Statin should be considered if the LDL cholesterol is >100 mg/dl with an LDL treatment goal of <100 mg/dl. An LDL treatment goal of <70 mg/dl is optional. For diabetics with chronic kidney disease, a moderate protein restriction of 0.8 g/kg body weight per day has been shown to reduce the risk of progression of albuminuria/proteinuria and loss of GFR. Recent data also suggest that 'Mediterranean' diet with more fruits and vegetables, fiber, legume and nuts and lower intake of salt, refined sugar and meat-particularly red meat-may slow progression of kidney disease. For other dietary interventions in patients with chronic kidney disease please see the chapter on chronic kidney disease [37,38].

Dihydropyridine calcium channel blockers (CCBs): Dihydropyridine CCBs (e.g., amlodipine, felodipine) as a sole agent have been shown to increase proteinuria in the IDNT study but are thought to be safe if used in combination with an ACE-Inhibitor or ARB. In fact, the ACCOMPLISH study has demonstrated superiority with regards to progression of chronic kidney disease of the combination of an ACE-Inhibitor with a dihydropyridine CCB as compared to the ACE-Inhibitor combined with hydrochlorothiazide.

Diuretics: Diuretics and RAAS inhibitors are synergistic in terms of effect on BP, i.e., the combined effect of agents from these classes on BP is equal to or greater than the sum of individual effects of each medication. Patients with diabetes and normal or near-normal GFR usually respond to thiazide-type diuretics. In the diabetic subgroup of ALLHAT, chlorthalidone reduced the primary endpoint of fatal coronary heart disease and myocardial infarction to the same degree as lisinopril or amlodipine and was superior for prevention of heart failure [39].

Non-dihydropyridine calcium channel blockers (CCBs): Non-dihydropyridine CCBs (e.g., diltiazem, verapamil) reduce proteinuria in short-term studies but have not been demonstrated to prevent the development or progression of DKD or cardiovascular disease. Non-dihydropyridine CCBs tend to have less potent effects on BP than dihydropyridine CCBs.

Beta blockers: Beta blockers have proven benefit for comorbidities that often accompany diabetes, including coronary artery disease, stroke, and congestive heart failure, and are often indicated for these conditions. In the absence of these conditions, the utility of beta blockers for BP control in diabetes is not clear. Beta blockers and RAAS inhibitors are not synergistic in terms of effect on BP, i.e., the combined effect of agents from these classes on BP is often less than the sum of individual effects of each medication [40,41].

Conclusion

Poor compliance, at any point of life creates serious mischiefs. Bangladesh is a country where poor literacy and carelessness never even gives opportunity to the general people to know the reasons behind their health complexities due to non-compliance and non-adherences. The most important thing is patient education, that the modern world is giving the highest priorities. Rich or poor, privileged or unprivileged all segment of population should be brought under the arena of compliance through patient education, at least by health campaign. Both government and profit taking medicine companies should take initiatives regard.

Competing Interests

The authors declare that they have no competing interests.

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