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Review Article

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 expenditure and imposes a huge economic burden on the healthcare systems. The International Diabetes Federation estimated more than 7 million people with diabetes in Bangladesh and almost an equal number with unexplored diabetes. This number is estimated to double by 2025. It is a costly condition and may cause 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 taken treatment from an unqualified provider. These are mostly because concern over medical costs, and pronounced socioeconomic disparities found for care-seeking behavior in both urban and rural Bangladesh.

Keywords: Diabetic Patient; Glycemic Control; kidney Function; Stroke; Blood Sugar; Albuminuria

Abbreviations: ADA-American Diabetes Association; ACCOMPLISH-Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension; ALLHAT-Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; ACE-Angiotensin converting enzyme Inhibitors; ARBs-Angiotensin Receptor Blockers; BIRDEM-Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders; CDiC-Children and adolescent in Changing Diabetes in Children; CCBs-Calcium Channel Blockers; CAD-Coronary Artery Disease; CVD-Cardiovascular Disease; CHF-Congestive Heart Failure; DM-Diabetes Mellitus; DAB-Diabetic Association of Bangladesh; DN-Diabetic Nephropathy; NIDDM-

Non-insulin Dependent Diabetes Mellitus; CKD-Chronic kidney disease; DKD-Diabetic Kidney Disease; ESRD-End Stage Renal Disease; eGFR-estimated Glomerular Filtration Rate; ESAs-Erythropoiesis Stimulating Agents; MGN-Membranous Glomerulonephritis; FCPD-Fibro-Calculous Pancreatic Diabetes; HbA1C-Hemoglobin A1C; IDNT-Irbesartan Diabetic Nephropathy Trial; IgA-Immunoglobulin A; FSGN-Focal Sclerosing Glomerulonephritis; IDF-International Diabetes Federation; HD-Hemodialysis; SPRINT-The Systolic Blood Pressure Intervention; RAAS-Renin-Angiotensin-Aldosterone System; SGLT2-Sodium-glucose co-transporter 2

1. Introduction

During 90s, 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 damaged. When the blood vessels in the kidneys are damaged, 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 undergo kidney failure. The primitive 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. DKD is a progressive condition and is the chief cause of 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 microalbuminuria should be treated with a most factual arbitration to retard the progression of DKD.

2. 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 pharma 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.

3. Results and Discussion

3.1 General pathophysiology and prevalence of diabetes complications

CKD was defined in terms of kidney deterioration (albuminuria) and decreased kidney activities (decreased [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 DM globally affects approximately 20% of adults over the age of 65 years. DKD is one of the most frequent and dangerous complexity of DM2, affecting about one-third of the patients with DM2 [3]. The current 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 most common cause of ESRD in the USA. ESRD incidence due to Type 2 DN is 35%-50%, according to the US Renal Data System [5], The next most common cause is hypertension [6]. The third most common element is glomerulionephritis. The important subgroups of glomerulonephritis include: MGN, IgA nephritis, and FSGN. Among all the complexities of

diabetes mellitus, nephropathy is the diabetes-specific complication with the greatest mortality [7]. Recently, there appears to have been a blast in the incidence of DN, which is most often type II, or NIDDM. The increased incidence of NIDDM appears linked to a virtual predominant of obesity in the USA [8].

3.2 Prevalence of diabetes in Bangladesh

An estimated 10 million people in Bangladesh have diabetes [9]. WHO stated 83% population of age group 25-65 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 years. 33% people age over 35 are diabetic or pre-diabetic, less than 15% 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 more than 25% of population [13].

3.3 Diabetes patients in Bangladesh with renal dysfunction

Glomerulonephritis was found to be the preeminent cause of ESRD and DN was the second common cause. Hypertension was trivial associated co morbid disease [14]. As kidney function declines, patients develop complexities related to fluid overload, electrolyte and acid-base imbalances, and the build-up of nitrogenous waste products. To survive, some patients ultimately need hemodialysis 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]. Microalbuminuria was found in 24% of type 1 diabetes, 27% of FCPD, and nearly 70% of type 2 diabetes in CDiC clinic, BIRDEM [19]. In Bangladesh, the causes of CKD G5 (End-Stage Renal Failure) among 954 patients who were on HD in 2012-13 were chronic glomerulonephritis (25.5%), diabetic nephropathy (41%) and hypertensive renal disease (33%) [20].

3.4 Non-adherence to preventive and therapeutic lifestyle

DAB selected 374 type 2 diabetic patients diagnosed for at least one year. Non-compliant diet was 90% and exercise was 25%. Nearly 35% patients non-adhered to self-blood glucose monitoring, 70% to foot care and 6% had smoking habits. The main barriers to adherence to blood sugar monitoring was that they did not believe it is useful (65%) and barriers to do exercise were always being busy (45%) and coexisting diseases (10%) [21].

3.5 Diabetic forecast

Almost 10% 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 5% in 1995 to 2005 and nearly 10% in 2006 to 2010. IDF 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].

3.6 Healthcare spending for diabetes in Bangladesh

A recent study by World Bank found $160 per year in household expenditures 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 US$314. Based on this finding, it is estimated that the total annual burden of more than 5 million diabetic patients will be US$1.5 billion, which is a large burden for a developing country like Bangladesh [25]. In 2016, approximately 55, 703 diabetic individuals received in-hospital care, with an estimated 2, 641, 000 outpatient visits. The total annual estimated cost of diagnosed diabetes was approximately US$ 217.71 million [26]. The median monthly cost of diabetes maintenance was close to USD 10, approximately 10% of the median monthly income [27].

4. Recommendation

4.1 Diet modification, exercise and statins for blood pressure/sugar control

Glycemic control is critical for the management of kidney patients with diabetes. Blood pressure should be aggressively controlled. SPRINT trial should target (<120/80). Exercise interventions improve the overall functional status and quality of life which also improve hyperlipidemia. Resistance exercise reduces visceral and trunk fat mass, as predictors of hypertension [20]. KDIGO (global NGO developing and implementing evidence-based clinical practice guidelines in renal disease) recommends treatment for a blood pressure of <140/90 in absence of proteinuria and <130/80mm Hg in presence of proteinuria [28, 29, 30]. ADA recommends a HbA1C goal of <7%. Glycemic target should be higher for elderly patients with comorbidity issues [3, 31, 32]. Therapy with a Statin should be contemplated if the LDL cholesterol is >100 mg/dl with an LDL treatment goal of <100 mg/dl. A modest protein limitation of 0.8 g/kg body weight per day has found to be advantageous to control albuminuria/proteinuria and loss of GFR. Diet modification is more accepted than diet restriction. Fruits, fiber and vegetables are encouraged as well as red meat and refined sugar opposed [33, 34].

4.2 Combination therapy

The first-line treatment options for hypertension in people with type 1 diabetes are ACE-Inhibitors or ARBs (for both type 1 or 2 diabetes). Diuretics or/and calcium channel blockers can 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 [35].

4.3 Use of RAAS inhibitors and diuretics

The RAAS plays a vital role in the pathogenic progression of DKD. 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. Aldosterone antagonists (Spironolactone) and direct renin inhibitors (Aliskerin) reduce proteinuria but they cannot prevent progression of DKD or CVD [36, 37]. Diuretics and RAAS inhibitors are co-operative in terms of effect on BP. In the diabetic subgroup of ALLHAT, chlorthalidone

reduced the primary endpoint of detrimental coronary heart disease and myocardial infarction to the same degree as lisinopril or amlodipine and was supercilious for prevention of heart failure [38].

4.4 Dihydropyridine/non-dihydropyridine CCBs and beta-blockers

Non-dihydropyridine CCBs (e.g. diltiazem, verapamil) decline proteinuria in momentary studies but have not been revealed to prevent the advancement of DKD or CVD. Dihydropyridine CCBs (e.g. amlodipine, felodipine) as a chief agent have proved to increase proteinuria in the IDNT study. They are more potent in BP control (as demonstrated by ACCOMPLISH study) than the Non-dihydropyridine CCBs but more effective in combination with ACE inhibitors than ACE inhibitors with diuretics. Beta blockers have proven contribution for controlling comorbidities that often follow diabetes, including CAD, stroke, and CHF. In the absence of these conditions, the utility of beta blockers for BP control in diabetes is not clear [39].

4.5 SGLT2 inhibitors for type 2 DM

Empagliflozin has been found to reduce exacerbate DKD, where, Canagliflozin declines the albuminuria aggravation, 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) [40].

4.6 HbA1c control in DKD

Chronic kidney disease, ESRD and treatment with ESAs found to be beneficial for RBC turnover. Studies reveal that HbA1c levels may not be the sole predictor of glycemic control in patients with CKD or ESRD. With progressive GFR loss, typically <20 mL/min/1.73m2 or ESRD, insulin catabolism is diminished and gluconeogenic capability by the kidney is impaired. Therefore glucose-lowering therapy often requires diminution to avoid hypoglycemia [41].

5. 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.

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Animal and Human experiment: N/A

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Consent for Publication

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