

Epidemiological Status of Chronic Diabetic Complications in China

Jian-Ping Weng¹, Yan Bi²

¹Department of Endocrinology, The 3rd Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong 510630, China

²Department of Endocrinology, Drum Tower Hospital Affiliated to Nanjing University Medical School, Nanjing, Jiangsu 210008, China

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With the booming development of industrialization and urbanization, popularization of high calorie diet and sedentary lifestyle, and the rapid growth of aging, the prevalence of diabetes increased nearly 10 times during the past three decades in China.^[1-3] China has become the country with the largest number of people with diabetes and thus will face considerable challenge of chronic complications in the next 10–20 years. Diabetes-associated chronic complications, such as vision disorder, kidney disease, neuropathy, peripheral vascular disease, cardiopathy, and stroke, are the major causes of physical disability and mortality, making it a nonnegligible problem of social healthcare system. Therefore, it is of importance to summarize and update current prevalence and risk factors of diabetic complications in China, not only to establish the strategy of prevention and treatment to delay the development of chronic complications, but also to improve the living quality of patients and alleviate the burden of medical cost.

DIABETIC RETINOPATHY

Diabetic retinopathy (DR), a retinal vascular disorder that occurs due to diabetes mellitus (DM), is the leading cause of blindness in diabetic patients. A nationwide retrospective analysis concerning chronic diabetic complications of inpatients during 1991–2000, initiated by Chinese Diabetes Society (CDS), suggested that 34.3% diabetic patients had ocular disease (including cataract, background retinopathy, proliferative retinopathy, and blindness), of which 20.5% in type 1 diabetes (T1D) and 35.7% in type 2 diabetes (T2D).^[4] A meta-analysis including 19 epidemiologic studies of DR from 1991 to 2012 in China indicated that the prevalence are 23.0% (95% confidence interval [CI]: 17.8–29.2%) for any DR, 19.1% (95% CI: 13.6–26.3%) for nonproliferative

DR, and 2.8% (95% CI: 1.9–4.2%) for proliferative DR. It is noteworthy that the prevalence of DR in China demonstrated a regional difference, with a higher prevalence in rural than in urban area, and in North than in South.^[5] Recently, a prospective research from Shanghai First People's Hospital showed that the incidence rate of DR in diabetic patients during the 5-year follow-up was 46.89%.^[6] Even if in the patients with good glycemic control (HbA1c <7%), the 5-year DR progression rate was up to 32.23%.^[7]

DIABETIC KIDNEY DISEASE

Diabetic kidney disease (DKD) refers to the kidney damage caused by diabetes, usually with an estimated glomerular filtration rate (eGFR) <60 ml·min⁻¹·1.73 m⁻² or urinary albumin-to-creatinine ratio >30 mg/g over 3 months, which remains the major cause of end-stage renal disease. The estimated prevalence for DKD in the United States is 20–40%, and until date, there is no large-scale study of the epidemiological characteristics of DKD in China. According to the nationwide retrospective study on inpatients during 1991–2000, 33.6% diabetic patients were diagnosed with DKD (including early renal disease, clinical renal disease, renal failure, and uremia), of which 22.5% in T1D and 34.7% in T2D.^[4] Recently, there are two studies regarding the prevalence of DKD in T2D patients within communities, in which one study included 668 community patients with

Address for correspondence: Prof. Jian-Ping Weng, Department of Endocrinology, The 3rd Affiliated Hospital of Sun Yat-sen University, No: 600, Tianhe Road, Guangzhou, Guangdong 510630, China
E-Mail: wjianp@mail.sysu.edu.cn

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T2D and revealed that 41.0% patients had microalbuminuria, 6.6% patients had macroalbuminuria, and 15.7% had an eGFR $<30 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ without albuminuria.^[8] Another research screened 1487 community patients with T2D and suggested that the overall incidence of kidney disease was 41.31%, in which DKD (proteinuria or macroalbuminuria with DR), non-DKD (characterized by microscopic or macroscopic hematuria, proteinuria without neuropathy or retinopathy, urinary tract infection were excluded under both conditions), and renal failure accounted for 18.51%, 13.44% and 9.36%, respectively.^[9]

Additionally, a retrospective study analyzed 244 patients with T2D undergoing renal biopsy and found that in those with disorder in routine urine test or kidney function without a history of DKD, 8.2% had a pathologic diagnosis of DKD, 84.0% had nondiabetic renal disease, and 7.8% had DKD complicating nondiabetic renal disease. Patients with co-existing DKD and nondiabetic renal disease also had clinical features of both DKD and nondiabetic renal disease, which included a high prevalence of DR, a long duration of diabetes, proteinuria, hematuria, and rapidly progressive renal failure.^[10]

DIABETIC PERIPHERAL NEUROPATHY

Diabetic peripheral neuropathy (DPN) is defined as peripheral, somatic or autonomic nerve damage attributable solely to DM, and the most common one is distal symmetric polyneuropathy. Researches on DPN varied due to diverse clinical manifestation and different diagnostic criteria. The retrospective study on inpatients from 1991 to 2000 demonstrated that the prevalence of diabetic sensory neuropathy (including pain, numbness, hypersensitivity, hyposensitivity, single nerve paralysis, and palsy) was 60.3%, with 44.9% in T1D and 61.8% in T2D.^[4] Since then, three epidemiological studies reported the prevalence of DPN in outpatients with diabetes. In 2008, an survey analyzed diabetic outpatients in 12 Chinese hospitals using 10-g monofilament examination and 128-Hz tuning fork and found that the prevalence of DPN was 17.02% in the total population, 18.28% in the known DM group, and 6.35% in the newly diagnosed DM group, respectively.^[11] In 2009, a cross-sectional study of outpatients with T2D across different levels of hospitals in Jiangsu province used diabetic neuropathy symptom score combined with 10-g monofilament and 128-Hz tuning fork and showed that the prevalence of DPN was 42.8%.^[12] Recently, a nationwide screening tests on DPN carried out by CDS included 3883 diabetic patients from 21 hospitals, which combined the perception of ankle reflex, vibration, temperature, pressure, acupuncture, and neural electrophysiology as diagnostic criteria, and the results showed that the national prevalence of DPN was 52.97%.^[13]

CARDIOVASCULAR AND CEREBROVASCULAR COMPLICATIONS

Cardiovascular and cerebrovascular diseases are the most common macrovascular complications of diabetes. The

nationwide study on inpatients during 1991–2000 revealed that cardiovascular and cerebrovascular complications in DM patients were 15.9% and 12.2%, respectively.^[4] Recently, there were two large-scale cross-sectional studies regarding the macrovascular complications in T2D patients. One study aimed to assess the control levels of blood glucose, blood pressure, and blood lipids (3B study), and revealed that the incidence of cardiovascular disease (including stable/unstable angina, myocardial infarction, percutaneous coronary intervention, or underwent coronary bypass) was 14.6% and the prevalence of cerebrovascular disease (including ischemic stroke, hemorrhagic stroke, or transient ischemic attack [TIA]) was 10.1%.^[14] The other one was to investigate the national glycemic control in outpatients and manifested that 10.38% patients had coronary heart disease and 5.26% patients had cerebrovascular complications.^[15]

The development of macrovascular complication is closely associated with metabolic disorders. Data from epidemiologic studies of TIA in China exhibited that the proportion of TIA complicated with diabetes was significantly higher than that without diabetes (24.0% vs. 12.6%); meanwhile, the proportion of TIA complicated with hypertension (69.5%) and lipid disorder (42%) was even higher.^[16] In addition, 3B study showed that the proportion of T2D with hypertension, dyslipidemia, and combination of hypertension and dyslipidemia was 30%, 12.2%, and 29.8%, respectively. When compared with T2D patients only, the patients with hypertension and dyslipidemia were 6 times more likely to report a prior history of cardiovascular disease.^[14]

DIABETIC FOOT

Diabetic foot is defined as infection, ulceration, and/or destruction of deep tissues associated with neurological abnormalities and various degree of peripheral vascular disease in the lower limbs, which is a severe and lethal diabetic complication that frequently leads to amputation. Diabetic foot is usually complicated with peripheral vascular disease. The study on inpatients during 1991–2000 revealed that the prevalence of lower extremity vascular disease was 5.0%, with 2.6% in T1D and 5.2% in T2D.^[4] Epidemiologic studies showed that diabetic foot problems were more severe with more risk factors and more medical cost in Northern China.^[17] Recently, two studies evaluated the relationship between diabetic foot and amputation. One retrospective research displayed that the proportion of amputation caused by diabetic foot was 27.3%.^[18] Another study showed that of all patients with diabetic foot, 21.2% had neuropathic ulcers, 23.5% had ischemic ulcers, and 53.1% had neuro-ischemic ulcers. The overall rate of amputation of diabetic foot was 19.03%, and risk factors included smoking, long duration of diabetes, infection, revascularization, rest pain, foot deformity, ulcer history, and HbA1c.^[19] Diabetic foot is usually associated with worse prognosis. Since there are evidences illustrating that most diabetic foot cases are preventable, early diagnose, and intensive supervision and management are the best ways to improve its prognosis.

As International Diabetes Federation pointed out, the prevalence of diabetes in China is a wake-up call for the government and policy-makers to take action on diabetes. Although faced with the upcoming high incidence of chronic diabetic complications and multiple institutional obstacles, health care providers have already made positive actions. Recent cross-sectional surveys showed that the ratio of Chinese T2D patients achieving the HbA1c target has improved.^[12,15,20] As it is an important basis for the national education of disease prevention and treatment, the priority is to develop strategies assisting more primary health care providers to recognize and treat diabetes. Chinese health care system is actively promoting the strategy with the grading system and is to divert patients with chronic diseases to the primary hospital. The experience of collaborations between tertiary and primary hospitals in Shanghai displayed that, after 3 year's integrated management, the rate of good glycemic control in diabetic patients and screening rate of chronic complications within community were significantly increased. Importantly, we noticed that the prevalence of diabetes-associated complications in the United States was significantly decreased based on activities in diabetes research and strategy during the past 20 years.^[21] These work, although still limited, have prompted us to believe that as we keep moving forward, we will make an impact on improving the lives of people with diabetes in the next 20 years.

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