


Diabetes: an overview of a rising epidemic

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Abstract

‘Diabetes’ is the term for diabetes occurring in the context of obesity. In this review, we will overview the latest epidemiological data available describing the rising prevalence, health impact and economic impact of diabetes. We will also outline the measures required to slowdown this newly evolving epidemic. The global prevalence of diabetes in 2010 was 284 million people

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Introduction

Diabesity is a new term describing diabetes in the context of obesity. Sometimes it is referred to as obesity-dependent diabetes. Recently, it has been recognized as a major public health problem that is evolving to become an epidemic [1–3]. In this review, we will discuss the epidemiology and impact of diabetes and obesity and how to combat this rising epidemic. The prevalence of both type 2 diabetes and obesity has had a rapid increase worldwide during the last century, mainly attributed to changes in human behaviour, especially sedentary lifestyle and dissemination of the western diet [4], in addition to genetic susceptibility [5–10]. Both diabetes and obesity are also integral components of metabolic syndrome [4,11,12].

Epidemiology of diabetes mellitus

The prevalence of diabetes has been persistently rising for the last few decades and it is being recognized as a worldwide epidemic [13]. The magnitude of the problem is reflected in Figures 1 and 2, which compare the estimates of the global prevalence of diabetes from the years 1995, 2000, 2010 and projection for the year 2030. It shows that the worldwide prevalence in the year 2010 is estimated to be 6.4% [13]. Between 2010 and 2030, there will be a net increase in the prevalence of diabetes among adults, as reflected by the 73% increase in adult diabetes numbers in developing countries, compared to 20% increase in developed countries [13]. Interestingly, these results show that the current prevalence of diabetes is much higher than the number projected before [13], which could also speculate a similar situation in the 2030s actual estimates.

Moreover, a recent study by Yang et al. was published in 2010 estimating the prevalence of diabetes among the Chinese population from June 2007 to May 2008 [14]. It included a representative sample of 46,239 adults, aged 20 years and older from 14 different providences [14]. Identification of undiagnosed diabetes was based on an oral glucose tolerance test (OGTT) showing a fasting glucose level ≥7.0 mmol/L (126 mg/dL) and/or 2-h glucose level ≥11.1 mmol/L (200 mg/dL), whereas those with previously diagnosed diabetes were identified based on self-report [14]. The age-standardized prevalence of diabetes was 10.6% among men and 8.8% among women, accounting for 92.4 million adults with diabetes (50.2 million men and 42.2 million women). In underdeveloped areas, the age-standardized prevalence of diabetes was higher among urban residents (10.4%) versus rural residents (5.8%) [14]. Moreover, the investigators showed a rising prevalence with increasing age and with increasing body mass index (BMI), confirming the relationship between obesity and diabetes in their cohort [14]. Other data showed that during the last 25 years, the prevalence of diabetes has doubled in the USA and multiplied by three to five times in India, Indonesia, China, Korea and Thailand [15]. Interestingly, regions with the highest comparative prevalence rates are North America (10.2%), followed by the
Middle East and North Africa (9.3%) [16]. The Pacific island nation of Nauru has 30.9% of its adult population living with diabetes, followed by the United Arab Emirates (18.7%), Saudi Arabia (16.8%), Mauritius (16.2%), Bahrain (15.4%), Reunion (15.3%), Kuwait (14.6%), Oman (13.4%), Tonga (13.4%) and Malaysia (11.6%) [16].

Health impact of diabetes mellitus

The major health impact of type 2 diabetes mellitus (DM) is due to its long-term complications including retinopathy, nephropathy, neuropathy, cardiovascular diseases, peripheral vascular diseases, stroke and periodontal pathologies [17]. Recent studies demonstrated that there is a reduction in health-related functioning associated with individuals with impaired fasting glucose, impaired glucose tolerance and type 2 DM when compared to those with normal glucose tolerance. This was in the form of increased bodily pain, reduced physical functioning, general health, mental health and vitality at baseline [18].

Eliminating diabetes was observed to extend both the overall life expectancy and the health-adjusted life expectancy for men by 1.3 and 1.4 years and for women by 2.0 and 1.7 years, respectively. Moreover, patients with diabetes had a significantly lower health-related quality of life in contrast to those without diabetes [19].

Economic impact

The burden of diabetes on the world economy has been increasing lately to reach at least $376 billion in 2010 and is expected to reach $490 billion in 2030. In 2010, it is estimated that ~12% of the health expenditures per person worldwide are expected to be spent on diabetes to reach $1330 per person [20]. This represents a significant economic burden as reflected by its consumption of 21, 16, 15 and 14% of the country’s total health expenditure in Saudi Arabia, Egypt, Mexico and USA, respectively (see Figure 3). In contrast, hypertension and its main sequelae, stroke and myocardial infarction, cost ~10% of the world’s overall health expenditure [21]. In the USA, the total expenditure on diabetes reached ~$41 billion in 2010, in contrast to $73 billion spent on all cancers combined, $96 billion on heart diseases, $63 billion on pulmonary conditions, $48 billion on hypertension, $19 billion on stroke and $65 billion on mental disorders [22]. Although developing countries are anticipated to have a 69% increase in prevalence by 2030 [13], 91% of the world total health expenditure on diabetes will be in developed countries while only 9% of the total will be in the developing countries [20].

In 2007, it was estimated that the burden of pre-diabetes and diabetes on the US economy reached $218 billion, $153 billion for higher medical costs and $65 billion for reduced productivity [23]. Moreover, the World Health Organization (WHO) announced that by 2025 India and China would have ~130 million diabetics consuming around 40% of their country’s healthcare budget.

Diabetes and end-stage renal disease

Chronic kidney disease (CKD) is a major complication of diabetes. Diabetes remains the leading cause of end-stage renal disease (ESRD) in most countries in the world, accounting for 40–50% of incident ESRD cases [24–26]. Recent studies showed the prevalence of CKD to be as high as 39.6 and 41.7% in patients with diagnosed and undiagnosed diabetes, respectively [27]. In contrast, CKD prevalence in those without diabetes is 10.6% [27]. Joyce et al. compared the direct cost of care before and after onset of ESRD for patients with and without diabetes [28] and concluded that the total adjusted annual costs per patient pre- and post-ESRD were significantly higher for diabetes (P < 0.0001) [28]. Adjusted annual costs per patient before and after diagnosis of ESRD were significantly higher for diabetes (P < 0.0001); annual costs were 69% ($38 041 vs $22 538) and 79% ($96 014 vs $53 653) higher pre- and post-onset, respectively [28]. In 2007, the mortality in the USA for patients with ESRD was 157.3 deaths per 1000 patients [29]. Moreover, the cost for ESRD in the USA was $35.32 billion in 2007 [29]. This empha-
sizes that diabetes and its closely related complication ESRD represent a huge economic and health problem. The high prevalence of ESRD among the diabetic population with its added substantial economic burden augments the problem even further to reach alarming levels.

Epidemiology of obesity

The WHO reports in 2005 indicate that the global prevalence of overweight adults (age 15+) (BMI 25–29.9 kg/m²) was ~1.6 billion and that of obese adults (BMI ≥ 30 kg/m²) was at least 400 million [11]. This accounts for one quarter of the world’s total population being at increased risk for developing cardiovascular disease, diabetes and eventually CKD. The projections for the year 2015 expect the prevalence of overweight adults to be as high as 2.3 billion and that of obese adults to be ~700 million. In 2005, the prevalence of being overweight among children younger than 5 years was estimated to be 20 million globally [11].

In the USA, the prevalence values varied according to age, sex, race and ethnic groups (Table 1). However, the previous trend of increasing obesity prevalence in the USA does not seem to be continuing at the same rate over the past 10 years, and this is more evident among women than men [30]. These values differ than those from other parts of the world as reflected by a recent study by Gigante et al. in 2009 on 49 395 individuals investigating the prevalence of obesity in Brazil, showing that the prevalence of overweight was 47% among males and 39% among females and that of obesity being around 11% for both genders [31].

The obesity epidemic is suggested to be due to the complex interaction of both environmental factors and genes [32]. It has been suggested that there are genes favouring storage of fat, which became maladaptive in our modern environment minimizing physical activity and favouring high-energy intake [32]. It has been found that obese children and adolescents are more likely to become obese in adulthood [33], and the risk rises even more if they have an obese parent [34]. Also, many studies have shown additive effects of genes on the body weight in the years following birth [35–37]. The recent changes in physical activities and nutritional behaviour including small snacks [38] and fast food (of the western diet) [39] are thought to be partly responsible for the increasing prevalence of obesity in children.

Health impact of obesity

Obesity is associated with increased risk for numerous chronic diseases including diabetes, hypertension, heart disease and stroke [40]. Obesity is also associated with various diseases including gastroesophageal reflux disease, colorectal polyps, colon cancer and liver diseases such as non-alcoholic fatty liver disease, cirrhosis and hepatocellular carcinoma [41]. Moreover, obesity and high BMI are associated with significantly reduced quality of life. The diabetes and coronary artery disease associated with obesity are also factors that contribute to the reduction of the quality of life [42]. Adams et al. reported that the risk of death is increased by 20–40% in overweight in-
diverticulosis and by 2-3 fold in obese individuals compared to normal weight individuals [43].

**Economic impact**

The health expenditure attributed to obesity alone in relation to a country’s total health expenditure varies globally reaching 0.7–2% [44,45] in France and 2.8–5.7% [45,46] in the USA, respectively [47] (Figure 3). When costs associated with being overweight were also included, the upper limit of this range rises to reach 9.1% of a country’s total healthcare expenditure [48]. Moreover, healthcare expenditures for morbidly obese individuals (BMI ≥40 kg/m²) are 81% higher than normal weight individuals (BMI = 18.5–24.9 kg/m²), 65% higher than overweight individuals (BMI 25–29.9 kg/m²) and 47% higher than individuals with class I obesity (BMI = 30–34.9 kg/m²). This higher expenditure was attributed to more frequent office-based visits, outpatient hospital care, inpatient care and prescription drugs [49]. In the USA, it is estimated that the total economic cost of obesity was close to $147 billion per year by 2008 [50]. The total indirect cost in the USA for 1999 was estimated to be ~$66 billion [51]. However, since the prevalence of obesity has increased substantially since 1999, the current costs are expected to be much higher. The annual medical spending because of overweight and obesity in the USA was ~$93 billion in 2002, constituting around 9% of the total health expenditure [52]. Furthermore, the USA total health expenditure on atherothrombosis including myocardial infarction, ischaemic stroke and peripheral arterial disease was $300 billion in 2004 [53].

**Recent advances**

**Chronic stress**

Recent studies by Gastaldi et al. in 2009 showed a significant contribution of chronic stress to the development of diabetes, through activation of the autonomic, neuroendocrine, inflammatory and immunologic systems [54]. It is thought that chronic psychological stress which characterizes the modern western daily life can in fact activate the hypothalamic-pituitary-adrenal axis to disturb the physiologic anabolic-catabolic hormonal balance, with downstream effect of increased visceral fat and insulin resistance [54]. Chronic stress is suggested to result in heightened neuroendocrine response with ensuing risk of developing pre-diabetes and cardiovascular diseases. Thus, targeting modifiable risk factors including stress management should be a cornerstone in therapy [54].

**Depression**

A recent case–control study conducted in 2010 on 296 newly diagnosed type 2 diabetes patients, who were matched on age and sex with 296 controls, investigated the association of depression with diabetes [55]. It consisted of 592 subjects with 432 (73%) men and 160 (27%) women aged between 25 and 60 years. The odds of mild depression among diabetic patients were 3.86 times the odds among controls [95% confidence interval (95% CI): 2.22–6.71], while the odds of moderate to severe depression among diabetic patients were 3.41 times the odds among controls (95% CI: 2.22–6.71) [55]. This indicates that there would be a higher incidence of various degrees of depression in those with type 2 DM. Depression was also associated with those with high BMI to include overweight and obese people [55]. Thus, it is suggested to begin screening for depression at an early stage with newly diagnosed diabetics [55]. This is further supported by previous literature showing up to three times higher risk of developing depression among diabetics in contrast to non-diabetics [56].

Another meta-analysis for over 15 longitudinal studies (n = 58 745) identified a direct reciprocal link between obesity and depression that is most evident in clinically diagnosed depression. It also demonstrated that this relationship is more evident in the American population, especially among adults. Obesity also increased the risk of developing depression in the future and vice versa; having clinically diagnosed depression was predictive of developing obesity and overweight [57].

**Challenges and opportunities**

The best way to contain this epidemic is to screen for early detection, prevention and early management of obesity, especially in younger individuals, before the development of type 2 DM. It was suggested that supplementation with micronutrients such as vitamin D and vitamin E could attenuate the innate immunity [58]. This could be achieved by fortifying the food with these micronutrients besides including high vitamin D and vitamin E diet in the daily meals of the school children, which needs a national plan, especially in developing countries. It is thus recommended that all individuals 30 years of age or older with risk factors should be screened annually for type 2 DM and obesity [59]. Risk factors include family history, hypertension, obesity, sedentary lifestyle, cardiovascular disease and hyperlipidaemia [59]. Screening should be done for high risk individuals using fasting plasma glucose (FPG). A patient with FPG ≥126 mg/dL (7.0 mmol/L) should be retested on a different day to confirm the diagnosis. An FPG <126 mg/dL (7.0 mmol/L) in an individual with a high suspicion for diabetes should be followed by a 75 g OGTT, where a 2-h post-load value ≥200 mg/dL (11.1 mmol/L) confirms diabetes [60]. This is further supported by the fact that at the time of diagnosis, 50% of patients have microvascular complications (retinopathy, neuropathy or nephropathy) and twice the risk of macrovascular complications when contrasted to the general population [61]. As for obesity, there is mounting evidence that the BMI (weight in kilogram/height in meter squared) is reliable and valid for detecting obese and overweight individuals with increased risk for morbidity and mortality [62]. Moreover, counselling obese individuals about diet, exercise and behavioural interventions (skill development, motivation and support strategies) produces modest sustained weight loss (3–5 kg for ≥1 year) [62]. A recent study by Lu et al. suggested that HbA1C can aid in the screening for DM in addition to its
We can conclude with what Hamlet said to his mother after he killed Polonius:

‘I must be cruel only to be kind;
Thus bad begins, and worse remains behind.’

*The Tragedy of Hamlet, Prince of Denmark,* by William Shakespeare, Act 3; Scene 4

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References

Glomerular diseases and transplantation: similarities in pathogenetic mechanisms and treatment options

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Abstract
Glomerular diseases and renal transplantation have always been considered as independent fields of nephrology, due to the supposed prevalent role of antibody production and immune complex formation in glomerulonephritis versus a direct reaction of immune cell towards the grafted kidney. However, both conditions share common pathogenetical pathways, and possible new therapeutic approaches are being envisaged. Innate immunity, particularly Toll-like receptors, dendritic cells and complement pathways, B cells and antibody networks are involved in the development of glomerular damage as well as graft injury. Consequently, new treatments targeting previously not considered immune pathways, like nuclear factor-κB or the proteasome and B-cell activation with antibody production, are being tested in glomerular diseases and in transplanted kidneys.

Keywords: B cells; glomerulonephritis; innate immunity; renal transplantation; treatment

Introduction
Glomerular diseases and renal transplantation have always been considered as independent fields of nephrology. This concept has been supported by the prevalent role of antibody production and immune complex formation in glomerulonephritis (GN) versus being due to the direct reaction of immune cells towards the grafted kidney. However, recent investigations have shown that the pathogenetic mechanisms operating in both conditions share common pathways offering some new therapeutic approaches iden-