Original Article

Prevalence of diabetes mellitus and population attributable fractions for coronary heart disease and stroke mortality in the WHO South-East Asia and Western Pacific regions

Asia Pacific Cohort Studies Collaboration[1]

The aims of this study were to obtain the most recent representative data for the prevalence of diabetes in adult populations in the World Health Organisation's South-East Asia and Western Pacific regions and to quantify the contribution of diabetes to the burden of mortality from cardiovascular diseases in these regions. Previous reports indicate that there are 83 million individuals with diabetes in the Asia-Pacific region, but since many of the country-specific estimates were not from nationally representative studies, this figure may not accurately reflect the current burden of diabetes. Information on the prevalence of diabetes was obtained by searching Medline and government health websites. Data were available from 12 countries representing 78% of the total population of the Asia-Pacific region. Six of 10 countries with complete data reported a prevalence of diabetes exceeding those estimates currently cited by the World Health Organization; three of which have also already exceeded the World Health Organization projections for 2030. In the 12 countries in the region with nationally representative data, the prevalence of diabetes ranged from 2.6% to 15.1%. Hazard ratios from the Asia Pacific Cohort Studies Collaboration were used to calculate population attributable fractions for diabetes for fatal cardiovascular diseases in the region. Population attributable fractions ranged from 2% to 12% for coronary heart disease, 1% to 6% for haemorrhagic stroke, and 2% to 11% for ischaemic stroke. Accurate estimates of the prevalence of diabetes are of great importance and standard methods are needed for periodic surveillance across the Asia-Pacific region and elsewhere.

Key Words: diabetes mellitus, Asia, Pacific Islands, prevalence, cardiovascular disease, stroke

Introduction

It has been estimated that there are currently 171 million people with diabetes worldwide, with 83 million of these individuals living in countries of the World Health Organization's (WHO) South-East Asia and Western Pacific regions (Asia-Pacific region).[1] Recent projections suggest that these figures will double by the year 2030 with the greatest burden of diabetes occurring in the Asia-Pacific region, where more than half of the world's population resides.[1] In addition, the latest report from the WHO on chronic diseases predicts that deaths from diabetes in the WHO South-East Asia and Western Pacific regions will increase by 39% and 51%, respectively, over the next decade.[2] Since diabetes is a major risk factor for cardiovascular diseases (CVD), reliably estimating the burden of CVD attributable to diabetes could be important in stimulating efforts for its primary prevention.

Previous studies estimating the prevalence of diabetes for each country in the Asia-Pacific region for year 2000 used data that were not always nationally representative of the surveyed countries.[1,3] Moreover, for the majority of countries for which there were no data, such as Kiribati and Vanuatu, estimates were made by extrapolating from the geographically closest, or socioeconomically and ethnically most comparable, country, which in this instance, was Fiji.[1,3] Such estimates represent best possible data but are, of course, not ideal. For example, the strength of the relationship between body size and diabetes may differ across ethnic groups, such that, for a given measure of adiposity, the risk of diabetes is greater among Indians than it is for natives of the Pacific Islands.[4] This is an important distinction given that adiposity is a risk factor for diabetes as well as CVD.

The first aim of the present study was to obtain the most recent representative data for the prevalence of type-2 diabetes in adult populations in countries of the WHO Asia-Pacific region. We then sought to quantify the direct impact of diabetes on the burden of CVD mortality by estimating population attributable fractions (PAF) for coronary heart disease, haemorrhagic and ischaemic stroke. This is the first study to use country-specific estimates for the prevalence of diabetes from the literature, together with hazard ratios for CVD derived from the local population via the Asia Pacific Cohort Studies Collaboration (APCSC) to calculate PAF

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for the region. The APCSC combined data on over 600,000 participants from 44 cohort studies in the region, to study chronic diseases and their risk factors in the Asia-Pacific region.

Materials and Methods

Information on the prevalence of type-2 diabetes among adults in countries of the WHO Asia-Pacific region was obtained by searching Medline with combinations of the MeSH terms: diabetes mellitus, metabolic syndrome, South Eastern Asia, Western Asia, Far East, Pacific Islands, Oceania and with each of the individual country names. Hong Kong and Taiwan were also included in the search terms and their results presented separately from mainland China since they have independent health, political, and administrative bodies, although they are not recognised as countries by WHO. References from relevant articles were scanned to obtain studies that may not have been indexed in Medline and additional studies were obtained by searching government health websites. National surveys and cross-sectional studies were selected for inclusion if they met the following criteria: (1) study samples were nationally representative of the adult (aged ≥ 18 years) population and (2) the 1999 WHO definition for diabetes was used, i.e. subjects with fasting plasma glucose (FPG) ≥ 7.0 mmol/L (126 mg/dL) or plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after 75-g glucose taken orally were classified as having diabetes.[5] One exception was allowed: Taiwan used fasting whole blood glucose ≥ 6.1 mmol/L, which is equivalent to FPG ≥ 7.0 mmol/L.[6]

PAF (%) of coronary heart disease, haemorrhagic stroke, and ischaemic stroke due to diabetes were calculated for each of the countries with data on the prevalence of diabetes using the formula.[7]

$$PAF = \frac{100 \times prevalence \times (HR-1)}{100 + prevalence \times (HR-1)}$$

Hazard ratios (HR) for diabetes, adjusted for age and stratified by sex and study, were obtained from the current database of the APCSC,[8] using Cox proportional hazard regression models. Statistical heterogeneity between countries was tested through adding interaction terms to the Cox models. As there was no evidence of heterogeneity (p>0.10), for any of the three outcomes, the same hazard ratios were used to calculate the PAF for all countries. In the APCSC, prevalent diabetes was defined by self-report or, where data on glucose were available, diabetes status was positive if fasting glucose was ≥ 6.1 mmol/L for serum samples, and ≥ 7 mmol/L for plasma samples, or if non-fasting glucose was ≥ 10 mmol/L for serum samples, and ≥ 11.1 mmol/L for plasma samples.[8]

Results

Nationally representative data on the prevalence of diabetes were obtained for 12 out of 40 countries (including Hong Kong and Taiwan) in the Asia-Pacific region. These countries make up 78% (2.65 billion individuals) of the total population in the region (Table 1). The diabetes prevalence data were obtained from studies conducted between 1993 and 2004, and varied in size, ranging from approximately 1,000 to 100,000 individuals. The age limits for inclusion also varied among studies. Except for Australia and Mongolia, all studies included in this report are new or updated compared with those used to produce the WHO 2000 estimates and 2030 projections.

A high prevalence of diabetes was observed in the Pacific Island country of Tonga (15.1%) and a low prevalence (<5%) was observed in India, the Philippines, Mongolia and China (Fig 1). The prevalences were higher in males than females in Australia, the Philippines, Singapore and South Korea and the opposite is true in China, Mongolia, Taiwan, Thailand and Tonga. The sex ratio for diabetes was around unity for Hong Kong, India, and Malaysia. Thus, no systematic male or female preponderance was observed for the Asia-Pacific region in this study.

Table 1. Summary of the most recent national representative studies for countries in the Asia-Pacific region

Country	Study year	Study size	Age (years)	Definition of diabetes
Australia[9]	1999-2000	11,247	≥25	FPG ≥ 7.0 mmol/L, 2hPG ≥ 11.1 mmol/L, previously diagnosed or on medication
China[10]	2002	98,509	≥18	FPG ≥ 7.0 mmol/L, 2hPG ≥ 11.1 mmol/L, previously diagnosed or on medication
Hong Kong[11]	1994-1996	2,893	25-74	FPG ≥ 7.0 mmol/L, 2hPG ≥ 11.1 mmol/L or on medication
India[12]	1999-2002	18,363	≥25	FPG ≥ 126 mg/dL and/or 2hPG ≥ 220 mg/dL
Malaysia[13]	1996	20,028	≥30	2hPG ≥ 11.1 mmol/L or previously diagnosed and on medication
Mongolia[14]	1999	2,996	≥35	2hPG ≥ 11.1 mmol/L
Philippines[15]	1998	4,541	≥20	FPG > 125 mg/dL
Singapore[16]	2004	4,168	18-69	2hPG ≥ 11.1 mmol/L, and previously diagnosed and on treatment
South Korea[17]	1998	7,962	≥20	FPG ≥ 126 mg/dL or previously diagnosed
Taiwan[18]	1993-1996	2,585	≥20	Fasting whole blood glucose ≥ 6.1 mmol/L or on medication
Thailand[19]	2000	5,105	≥35	FPG ≥ 126 mg/dL or previously diagnosed
Tonga[20]	1998-2000	1,024	30-64	FPG ≥ 11.1 mmol/L and an elevated HbA level

† FPG = fasting plasma glucose, 2hPG = 2 hour post-load plasma glucose

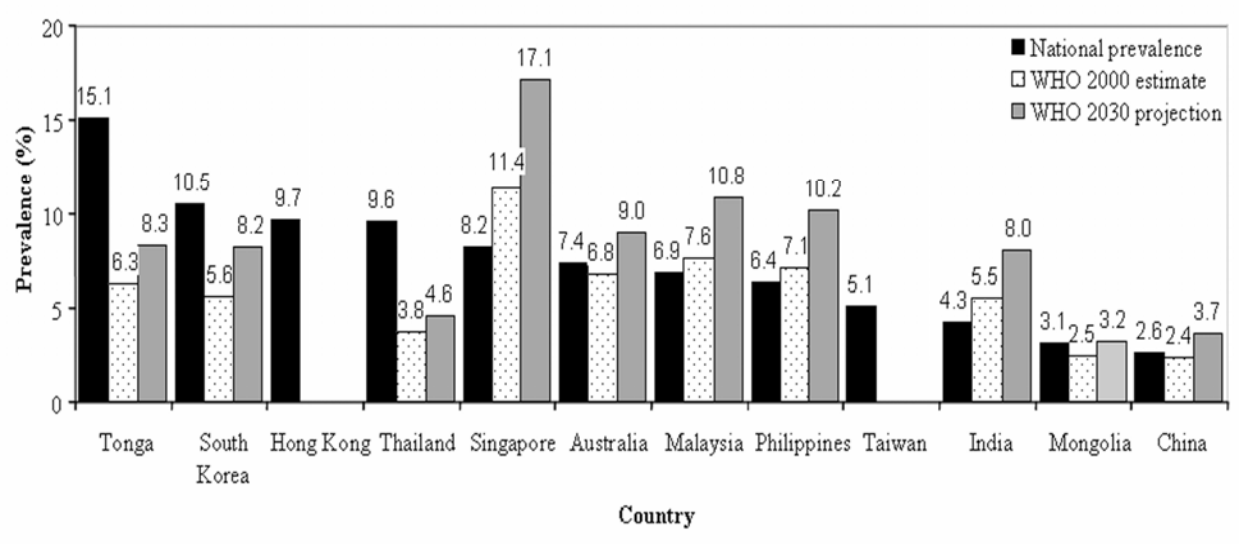

Figure 1. Prevalence of diabetes from national surveys, World Health Organization 2000 estimate and 2030 projection
Note that World Health Organization 2000 estimate and 2030 projection were not provided for Hong Kong and Taiwan.

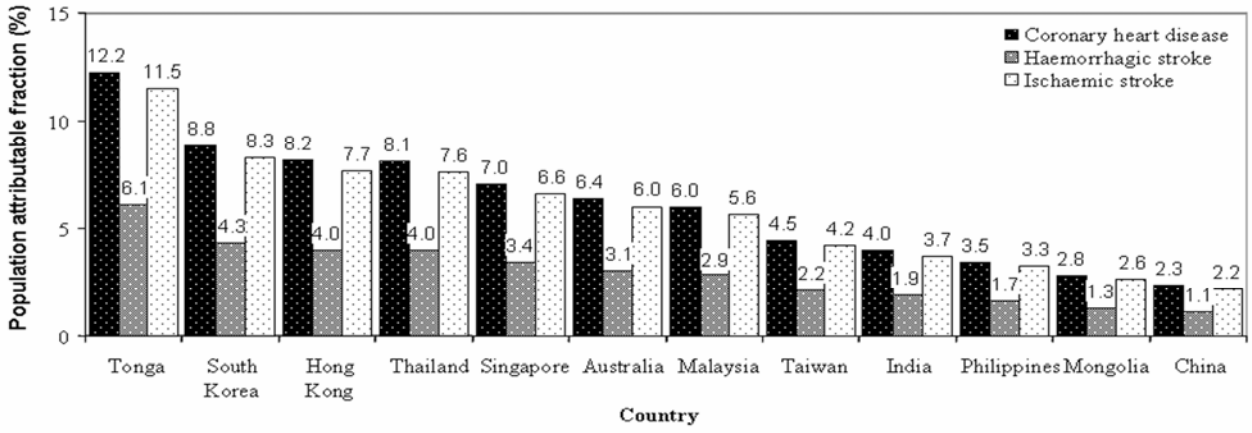

Figure 2. Population attributable fractions of fatal coronary heart disease, haemorrhagic stroke, and ischaemic stroke due to diabetes in the Asia-Pacific region

The hazard ratios (95% confidence intervals), adjusted for age and stratified by sex and study, from APCSC were: 1.92 (1.68-2.19) for fatal coronary heart disease, 1.43 (1.05-1.95) for fatal haemorrhagic stroke, and 1.86 (1.29-2.69) for fatal ischaemic stroke. The PAF for fatal CVD associated with diabetes were highest in Tonga and South Korea, and lowest for China and Mongolia (Figure 2). Overall, the PAF ranged from 2.3%-12.2% for coronary heart disease, 1.1%-6.1% for haemorrhagic stroke, and 2.2%-11.5% for ischaemic stroke.

Discussion

This current review of the most recent nationally representative data for the prevalence of diabetes in the Asia-Pacific region demonstrates that previous reports underestimate the actual prevalence of the disease. In six out of 10 countries (excluding Hong Kong and Taiwan since WHO estimates were not provided for these two areas), the prevalence of diabetes exceeded the WHO country-specific estimates for the year 2000. Indeed, the current prevalence derived from national data for South Korea, Thailand, and Tonga already exceeds the projected figure for adults (aged ≥ 20 years) for these countries in 2030. It could be argued that, since the surveyed populations included in the current study for Thailand and Tonga were aged ≥ 35 years, these values overestimate the burden of diabetes within these countries, since diabetes typically develops in mid-life. However, as the current prevalences reported here are almost double those projected for 2030, this is unlikely a complete explanation. A more reasonable explanation for the conservative projections for 2030 for these countries is that these projections were extrapolated from studies conducted between 1989 and 1992, which had baseline prevalences much lower than the more recent prevalences reported here. In addition, we have used only nationally representative in-country data whilst the WHO used data from neighbouring countries (Thailand and Tonga estimates were obtained from Singapore and Samoa data, respectively) or a region of the country (South Korea estimates were not national but instead derived from Yonchon County.).[1]

In contrast, the WHO 2000 estimate and 2030 projection for Singapore were derived from the Singapore National Health Survey 1992, which reported a

prevalence of 8.6%.[16] Whether based on projections[1] or data on temporal trends in prevalence[21], all indications are that the burden of diabetes in the region will only worsen. However, following public health initiatives,[16,22] the prevalence of diabetes in Singapore was reported to have decreased significantly ($p<0.05$) from 9.0% to 8.2% during the period 1998-2004.[16] If this trend continues, or at least stabilises, then the WHO 2030 projection of 17.1% for Singapore will be a considerable overestimate.

Furthermore, regional[23] and solely urban[24,25] studies in India have suggested a higher prevalence than that reported in this study, based on a nationally representative study. However, even if the national prevalence of diabetes in China and India are lower than most countries in the region, these two countries have the largest total number of people with diabetes, of 22 million and 20 million, respectively. The country with the third largest total number of people with diabetes, South Korea, has five times fewer people with diabetes than China and India. This clearly illustrates the scale of the existing diabetes problem in these two nations.

The PAF for the three fatal cardiovascular outcomes due to diabetes varied from 1-2% in China to 2-4% in India and 6-12% in Tonga. For reasons of brevity, we have restricted calculation of PAF to cardiovascular outcomes in this paper. However, APCSC[8] also showed significant associations between diabetes and fatal outcomes for renal disease (hazard ratio: 2.93), cancer (hazard ratio: 1.21), respiratory infections (hazard ratio: 1.52), all infections or inflammatory disease (hazard ratio: 1.98), all non-cardiovascular disease (hazard ratio: 1.56), and all-cause mortality (hazard ratio: 1.68); hence the fractions for these outcomes attributable to diabetes or related conditions will also be substantial in the region. For example, there were approximately 370,000 deaths from all-cause in Thailand in 2001[26] and the PAF of all-cause mortality due to diabetes was 6%, therefore, approximately 20,000 deaths in Thailand may be attributable to diabetes.

This study only reported the prevalence of diabetes and did not consider the prevalence of impaired glucose tolerance and impaired fasting glucose, even though people with impaired glucose tolerance or impaired fasting glucose are at high risk of developing diabetes.[27] Our omission reflects the lack of studies on the hazard ratios for impaired glucose tolerance and impaired fasting glucose; and impaired glucose tolerance or impaired fasting glucose are not yet considered to be independent disease entities separate from diabetes. Hence, the estimates reported here are likely to be an underestimate of the true burden of diabetes-related illness. In fact, some of the countries selected for this study had higher prevalences of impaired glucose tolerance and impaired fasting glucose than for diabetes.[11,12,14,16]

A limitation of this paper is that studies from only 12 countries were used in this report, since other available studies did not use the 1999 WHO definition of diabetes or their data were not nationally representative. However, since the population in these 12 countries represents 78% of the total population in the Asia-Pacific region, this should not have a significant impact on our understanding of the role that diabetes has on CVD. Other limitations include differences in the year of data collection and inconsistencies between countries for the definitions of adult used for diabetes prevalence estimates. This precludes the direct comparison of diabetes prevalence between countries. As well, age-standardization was not possible because of lack of systematic information from the datasets. The use of the same hazard ratios to derive country-specific PAF in this study was a limitation, and the lack of significant differences in hazard ratios between countries may be due to sampling error. A further limitation is that APCSC does not include studies from India and Pacific Island countries,[8] due to the lack of eligible cohorts. Additionally, because the prevalences of diabetes were not age-standardized, the inter-country variation of the PAF can be partly due to differences in the age distribution in the populations studied.

The continuing urbanisation, growth and ageing of the population, in many lower and middle-income countries, including the world's two most populous nations, China and India, will ensure that the epidemics of diabetes and CVD are likely to increase substantially unless effective interventions are introduced on a wider scale. Consequently, accurate measurement of the prevalence of diabetes is of great importance. Standard methods (such as age range and definition of diabetes) are also needed for periodic surveillance in the Asia-Pacific region and worldwide.

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Original Article

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Asia Pacific Cohort Studies Collaboration

世衛組織東南亞及西太平洋地區的糖尿病盛行率及其對冠狀心臟病及中風死亡率的可歸因危險

本研究的目的為收集世界衛生組織東南亞及西太平洋地區最近之代表性資料已獲取成人族群糖尿病盛行率，並量化在這些地區糖尿病對心血管疾病死亡率負擔的貢獻。之前的報告指出在亞太地區有 830 萬人罹患糖尿病，但由於很多國家別的估計並非來自國家代表性的研究，這些圖像可能無法精確的反應目前糖尿病的負擔。糖尿病盛行率的資料來源是搜尋 Medline 以及政府衛生網站。其中有 12 個有資料的國家，代表 78%亞太地區的總人口。十個有完整資料的國家中，有六個其報告的糖尿病盛行率較世界衛生組織目前引述的數據高；其中有三個國家已經超過世界衛生組織推估 2030 年的盛行率。在有全國代表性樣本的 12 個國家中，糖尿病的盛行率範圍從 2.6%至 15.1%。亞太地區世代研究合作小組，計算這個地區的糖尿病對於致死性的心血管疾病之可歸因危險性以危害比表示。人群可歸因危險分率的範圍：冠狀動脈疾病由 2%至 12%，出血性中風 1%至 6%，缺血性中風 2%至 11%。為了定期監測亞太地區及其他地區，準確的評計糖尿病的盛行率是非常重要的，我們需要標準的方法。

關鍵字：糖尿病、亞洲、太平洋群島、盛行率、心血管疾病、中風。