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Diabetes in South-East Asia: An update

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ABSTRACT

According to the recent estimates by the International Diabetes Federation (IDF), South East-Asia (SEA) Region consisting of India, Sri Lanka, Bangladesh, Bhutan, Mauritius and Maldives, is home to more than 72 million adults with diabetes in 2013 and is expected to exceed 123 million in 2035. Nearly 95% of people with diabetes have type 2 diabetes (T2DM). Although type 1 diabetes (T1DM) is relatively rare in these countries, its prevalence is also rising. Furthermore, a large number (24.3 million) of people also have impaired glucose tolerance (IGT). Several characteristic differences are seen in the clinical and immunological presentation of these people when compared with their European counterparts.

A sharp increase in the prevalence of T2DM has been observed in the SEA Region, both in urban and rural areas, which is mostly associated with the lifestyle transitions towards urbanisation and industrialisation. Evidence suggests that a large portion of T2DM may be preventable by lifestyle modification. However, morbidity and early mortality occur as a result of inadequate healthcare facilities for early detection and initiation of therapy, as well as suboptimal management of diabetes and associated morbidities. This is largely preventable by primary prevention of diabetes and enhancing awareness about the disease among the public and the healthcare providers. There is an urgent need for concerted efforts by government and non-governmental sectors to implement national programmes aimed at prevention, management and surveillance of the disease.

1. Introduction

The global prevalence of diabetes, and especially type 2 diabetes (T2DM), is increasing at an alarming rate. According to the recent update by the International Diabetes Federation (IDF) more than 382 million adults aged 20–79 years had diabetes in 2013 [1]. The prevalence is increasing in every country, and major economic, social and healthcare impacts will be seen in developing countries, as these countries are home to as much as 80% of people with diabetes [1].

Prevalence estimates of diabetes and Impaired Glucose Tolerance (IGT) are high for all South-East Asia countries and are expected to increase further in the next two decades [2]. The South-East Asia (SEA) Region is estimated to have more than 72 million adults with diabetes and 24.3 million with IGT.

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The present trend indicates that more than 60% of the world's population of people with diabetes will be in Asia. The number of people with diabetes will exceed 123 million in 2035 unless drastic steps are taken to curb this trend [1].

2. Epidemiology

2.1. Rising prevalence of type 1 diabetes

The estimates of the global incidence of type 1 diabetes (T1DM) have mainly been based on limited epidemiological studies [3]. Given the relatively rare occurrence of T1DM in Asian populations, as well as the heterogeneity of phenotype in young people with diabetes, data collection has not been as systematic as those in Western countries, where national registries of patients with T1DM are available [3]. Most countries in Asia do not have established registries for T1DM, making data collection rather fragmented. Nevertheless, based on available data, there is clear evidence of an increase in prevalence and incidence for T1DM in the region, which is contributing to a narrowing of the polar-equatorial geographical variation in the prevalence of T1DM [3].

The clinical characteristics of T1DM among Asian patients are notable for several important differences. The age of presentation is in general older compared to that in Europeans, and a significant proportion have co-existing obesity, termed ''double diabetes'', which may mask the underlying diagnosis and complicate management [3]. In the Asian Young Diabetes (ASDIAB) Study of newly diagnosed diabetes among 12–40 year olds, classical T1DM accounted for only 10% of new presentations with diabetes [4]. In a study of 58 consecutive patients with T1DM in Kolkata in India, 33% were overweight (Body Mass Index (BMI) $> 23\ kg/m^2$), 10% were obese (BMI $> 27\ kg/m^2$), and 28% had central obesity [5]. The SEA Region has one of the highest estimates of prevalence of T1DM in children with 77,890 affected in 2013 [3]. According to the IDF estimates, India has the second highest number of children with type 1 diabetes (67,700) after the US and the largest proportion of incident cases of T1DM in children in the SEA Region is contributed by India [3].

Anti-insulin auto-antibodies are typically present only among 30–40% of patients with T1DM in Asia, compared to the reported prevalence of 70–80% in Western populations [6]. This may simply reflect differences in underlying pathophysiology. On the other hand, an increasing proportion of subjects treated as T2DM are recognised to have evidence of progressive autoimmune destruction of beta-cells, and fulfil a diagnosis of latent autoimmune diabetes in adults (LADA) [6].

2.2. Rising prevalence of type 2 diabetes

Epidemiological data indicate that the prevalence of diabetes has been rising in the SEA countries for at least two decades and current estimates have surpassed all previous predictions [1]. Most of these countries have large rural populations; therefore, rising trends in the rural areas would add huge numbers to the population of people with diabetes. The contributory factors for this phenomenon are described in a section below; the impact of these drivers has already been manifested in urban settings. Table 1 shows the latest urban and rural prevalence estimates of diabetes in SEA countries and the projected figures for 2035, as estimated by the IDF [1]. According to the 2013 estimates by the IDF, the highest prevalence in the SEA region is found in Mauritius (14.8%) followed by India (9.1%). India, Nepal, and Sri Lanka have higher numbers of people with diabetes in rural areas than in urban areas.

Long-term trends in prevalence of diabetes have been reported only from a few SEA countries. India, the largest country in the Region, has more than 65 million adults with diabetes and has the second highest number of cases in the world after China. A steady increase in prevalence has been noted both in the urban and rural areas [7]. Increasing life expectancy will also contribute greatly to the anticipated increase in regional diabetes prevalence in SEA. The proportion of the world population over the age of 60 is expected to increase from 12.2% to 17.6% between 2015 and 2035 [8] and the urban population will rise from close to 53.9% to 61.7% [9].

Various studies have highlighted that Asian Indians have a higher risk of diabetes compared to other Asian populations, whether they are living in their land of birth or in an affluent foreign country [10]. Furthermore, Asian Indians have a younger age at onset, lower BMI risk threshold level, and higher prevalence of Impaired Glucose Regulation (IGR) [10].

Mauritius, a middle-income country, has the highest prevalence of diabetes among adults in the region (14.8%)

Table 1 – Estimates of diabetes and impaired glucose tolerance (IGT) prevalence in adults (20–79 years), 2013 for the South-East Asia Region [1,2].

Country/territory	Age-standardised prevalence (%)	Prevalence cases in (1000s)	Number with diabetes in 1000s		IGT crude prevalence (%)
			Rural setting	Urban setting	
Mauritius	14.8	143.608	68.40	73.25	10.7
India	9.1	65,076.361	34,433.22	28,580.65	2.8
Sri Lanka	7.6	1128.008	793.45	306.76	5.5
Bangladesh	6.3	5089.042	1614.48	3906.93	2.5
Bhutan	5.8	22.502	10.55	11.81	2.7
Nepal	4.9	674.119	191.01	315.71	2.0
Maldives	4.8	7.881	6.56	9.34	4.3

and in 2010 the prevalence was the 4th highest globally [11]. A large proportion (68%) of the population is of Asian Indian origin. The diabetes prevalence has increased by 64% from 13.0% in 1987 to 21.3% in 2009 in adults [12]. The prevalence of IGT has increased by 3%, and the prevalence of impaired fasting glucose (IFG) by 12.6%. The elevated prevalence of IGT (10.3%) indicates a high potential for a further increase in number of people with diabetes.

2.2.1. *Urban and rural prevalence*

Although the prevalence rates are often higher in urban than in the rural settings, the rates are increasing more rapidly in the rural population [10,13]. A systematic analysis of long-term trends in diabetes in rural India in a 15 year period (1994–2009) showed an increase of a rate of 2.02 per 1000 persons per year [14].

Similarly, trends between 1989 and 2005 in one study showed a 2.2-fold increase in prevalence in urban populations from 8.3% to 18.6% and a 4.2-fold increase in the rural population from 2.2% to 9.2% [7]. In Sri Lanka, between 1990 and 2000, the prevalence of diabetes increased 1.2-fold from 5.3% to 6.5% in the urban population and 3.4-fold from 2.5% to 8.5% in the rural population [13].

2.2.2. *Regional disparities*

There are within-country regional disparities in prevalence rates from all the countries. A recent study from The Indian Council of Medical Research – INdia DIABetes (ICMR-INDIAB), conducted in 3 states and in 1 union territory (UT) representing 213.5 million people in urban and rural settings, from November 2008 to April 2010, showed that the weighted prevalence of diabetes in adults $\geq$20 years was 10.4% in Tamil Nadu (South), 8.4% in Maharastra (Central), 5.3% in Jharkhand (East) and 13.6% in Chandigarh (UT) and of prediabetes (IGT and/or IFG) was 8.3%, 12.8%, 8.1% and 14.6%, respectively [15]. Risk factors for diabetes and prediabetes included age, family history of diabetes, urban residence, abdominal obesity, hypertension and income status [15].

2.2.3. *Limitations of the studies*

Comparative studies within and between countries in SEA are difficult because of several shortcomings including: narrow regional focus, inadequate sample size, varied sample design, limited focus on rural population, lack of uniform methodology and diagnostic criteria, and lack of standardisation of study procedures. Efforts should be made to improve the quality of the data.

2.2.4. *Prediabetes*

The prevalence of prediabetes (IGT and IFG) is also high among the SEA populations, as shown in Table 1. More importantly, the conversion rate to diabetes is more rapid in SEA than in other populations [10,16,17]. Recent data from India [7,16] and a systematic review from south Asians living worldwide [18] indicated an overall increase in diabetes prevalence, but long term trends of IGT prevalence were less clear. Studies from Tamil Nadu, India and Mauritius have reported a decline in IGT prevalence with a concomitant rise in diabetes prevalence, which could be a result of a rapid conversion of IGT to diabetes. Systematic population-based longitudinal studies are required to understand the factors influencing the prevalence of various levels of glucose intolerance among South-East Asians.

2.2.5. *Gestational diabetes (GDM)*

A major issue in GDM research has been the varied criteria and screening methods used, causing wide variations in the prevalence rates within a country itself. In addition, a new definition released by the World Health Organization [19] will greatly affect the reported prevalence of GDM and diabetes first-detected during pregnancy [20]. A review of literature [21] has shown an increasing trend in the prevalence of GDM in some SEA countries and high prevalence in some communities. The highest rates of GDM (18%) have been found in urban women in Chennai, India, however, these rates are far higher than have been reported in other parts of the country [22]. Another recent review found that GDM rates were lower in SEA women compared to other Asian countries. However, GDM rates were higher in ethnically South-East Asian women born in SEA, compared to ethnically South-East Asian women born in the US, UK, or Australia [23].

3. Risk factors

The rising trend in diabetes prevalence in Asian countries in general and the SEA Region in particular, is associated with the risk factors shown in Fig. 1. Several peculiar genetic characteristics and acquired risk factors heighten the predisposition to the disease, and environmental and social conditions accelerate development of metabolic disorders. The adverse metabolic profile that is often seen in obese and elderly white populations is often manifested in young and non-obese SEA populations [10].

The SEA and Western Pacific Regions are now facing an epidemic of diseases associated with obesity, such as diabetes and cardiovascular diseases [24]. Increasing trend in overweight and obesity has been associated with the rising trend in diabetes in Chennai, India, both in the urban and rural populations [7]. Although the recent prevalence of overweight was lower in the rural (19.5%) than in the urban (40.0%) populations, the rise in the rural prevalence was nearly 8.6-fold higher than in the urban population over a period of 14 years.

Recent studies in India [7,16,25] and in Sri Lanka [13] demonstrate that T2DM is being diagnosed at a younger age in both urban and rural areas. The prevalence of T2DM in the young is increasing rapidly in SEA populations across the world. Compared with children of other ethnic origin, South-East Asian children manifest metabolic obesity, insulin resistance and metabolic perturbation at a younger age and of a greater magnitude [10].

4. Healthcare burden

Nineteen percent of people with diabetes live in SEA, yet one quarter of the 12 million deaths worldwide due to diabetes occur in this Region. More than 55% of people with diabetes in the region die under the age of 60 years [2]. Major contributory factors for development of complications include delayed

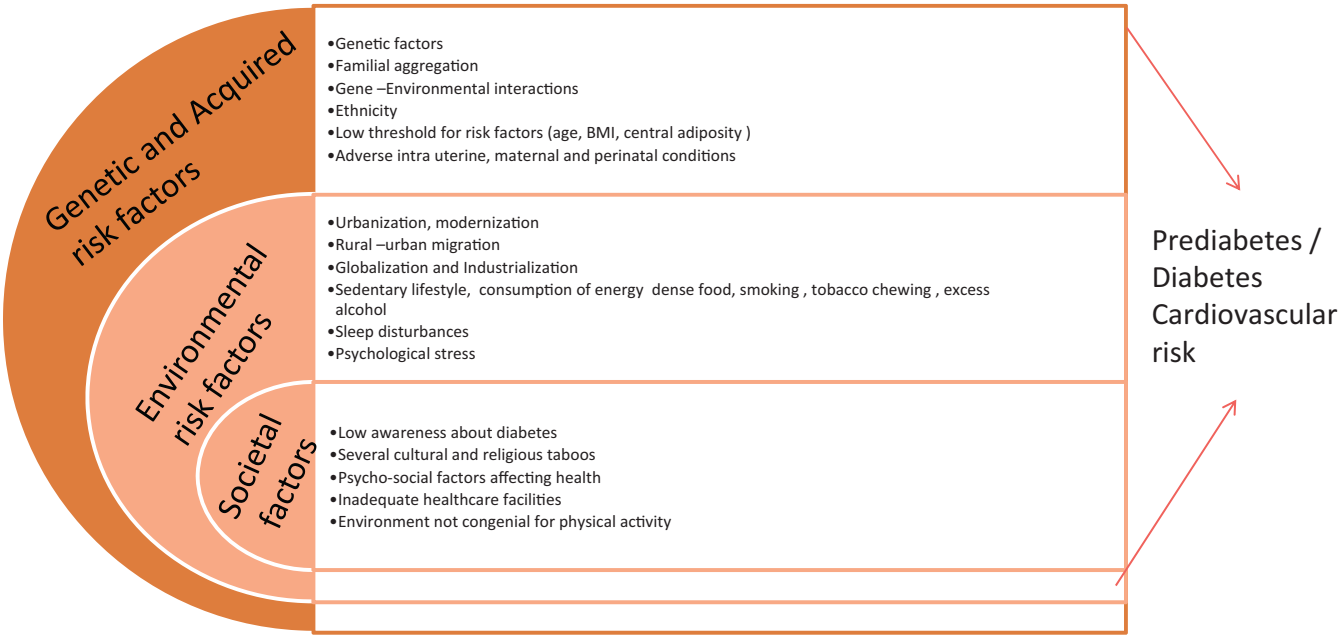

Fig. 1 – Possible etiological factors enhancing the predisposition to type 2 diabetes among South-East Asians.

diagnosis, sub-optimal control of glycaemia and hypertension, and inadequate medical facilities. There is a need for greater awareness of the benefits of early detection and tight control of diabetes, and strategies for primary and secondary prevention in diabetes are lacking even among the medical community. Optimal glycaemic control is achieved only in a small proportion of people with diabetes in SEA [26].

Unlike high income countries, in SEA lower socioeconomic status groups often have a lower prevalence of diabetes compared to higher socioeconomic status groups although this trend is changing. Many people in lower socioeconomic status groups may develop complications as they often tend to neglect diabetes care due to the high cost. People with diabetes in the lowest social stratum usually spend 25–34% of their income on diabetes care, which further increases dramatically when complications develop [10]. Furthermore, people with diabetes living in rural settings face increased difficulties, due to disparities in human and infrastructural healthcare resources.

4.1. *Healthcare organisation*

Despite the tremendous burden of diabetes and its complications within the SEA Region, there is a comparative lack of structured care management and integrated healthcare policies, thereby hindering the prevention, detection and management of diabetes and related co-morbidities. Thus, diabetes is often diagnosed late, presenting as acute medical emergency rather than through ambulatory care settings. Resource limitations mean that there is a general lack of trained personnel and a greater need for a team approach. Furthermore, in many of the developing countries, lack of infrastructure also means that there is limited access to medical services, especially in rural areas [27].

Several studies have highlighted the large proportions of people with diabetes with suboptimal glucose control or suboptimal risk factor management. In the International Diabetes Management Practice Study (IDMPS) [26], more than 11,000 subjects with diabetes were recruited from different countries of Asia, as well as from other developing regions. Only 37% of participants with T2DM from Asia achieved a glycaemic goal of HbA1c <7%, due to longer disease duration, microvascular complications, lack of self-monitoring and lack of insulin self-titration. In addition, there was an alarming paucity of control of other risk factors such as blood pressure and lipids. Overall, only around 40% of the recruited T2DM patients from Asia performed self-monitoring of blood glucose, and there was significant mismatch between patient risk factor control and physician perception.

Other factors which may contribute to the suboptimal diabetes care in Asian countries include less-developed integrated chronic care, the channelling of healthcare resources towards acute and advanced diseases, high use of complementary and alternative therapies, high rate of loss to follow-up of patients, and a low level of public awareness and public education [28]. To address this, several community awareness programmes have been developed to raise awareness of diabetes in the Region [29].

5. Morbidity and mortality

The evaluation of prevalence of complications in Asian countries has been hindered by the lack of national data, and there are only a few systematic comparisons between countries or people of different ethnic backgrounds. However, the research that has been conducted suggests that South Asians have a general predisposition to renal disease and cardiovascular disease compared to Europeans. Cardiovascular disease susceptibility has been attributed to visceral adiposity and the ‘‘thin-fat’’ phenotype of many Asian

populations [30]. In the Chennai Urban Population Study (CUPS), prevalence of coronary artery disease was present in 21.4% of subjects with diabetes, compared to 9.1% in subjects with normal glucose tolerance [31]. Studies conducted in the UK have also reported similar prevalence of coronary heart disease (CHD) among South Asians living in the UK, compared to whites [32]. Interestingly, this pattern of increased cardiovascular complications is not seen in East Asians, who also have a tendency to visceral adiposity [33]. A multi-ethnic study conducted in Singapore has noted a stronger association between diabetes and ischaemic heart disease among Asian Indians compared to Chinese and Malaysians [34]. Peripheral vascular disease was comparatively less common in South-East Asians, it was 6.3% among subjects with diabetes, and 2.7% in subjects without diabetes [35].

Microvascular complications appear less common among Asians compared to European populations. Diabetic retinopathy was present in 17.6% of subjects in Chennai, India [36]. The population-based cross-sectional Singapore Malay Eye Study found that diabetic retinopathy was present in 35% of subjects [37]. In the Joint Asia Diabetes Evaluation (JADE) Program, an electronic registry of patients with diabetes from several Asian countries including Korea, Thailand, Hong Kong, Singapore and India, the prevalence of diabetic retinopathy was 20.4% [38]. In a recent pooled analysis using data from population-based studies from around the world, it was noted that the prevalence of diabetic retinopathy was considerably lower among South Asians compared to Caucasian populations [39].

Furthermore, people with diabetes from Asia appear to be at increased risk for diabetic nephropathy. In India, the Chennai Urban Rural Epidemiology Study (CURES) found that the prevalence of microalbuminuria was 26.9% and overt nephropathy was 2.2% among T2DM subjects, and the main predictors of microalbuminuria were glycaemic control, duration of diabetes and blood pressure [40]. Incidence of End Stage Renal Disease (ESRD) was reported to be higher among Asians living in the UK [41] and the Netherlands [42] compared to Europeans.

These differences in the pattern of complications may be due to a variety of factors, including genetic factors, socio-economic factors, and healthcare structure which hamper early detection and intervention for the complications. Nevertheless, the Diabetes Study of Northern California (DISTANCE), among 64,211 people with diabetes, reported that Asians had a lower risk of lower-limb amputations, and had comparable rates of cardiovascular disease, with significant heterogeneity among the Asian subpopulations [43]. The risk of endstage renal disease (ESRD) was comparable among whites and South Asians. The ethnic difference in diabetes complications was not fully explained by demographic, socioeconomic, behavioural, and disease-related clinical outcomes, suggesting possible differences in genetic susceptibility [43].

In addition to the well-recognised vascular complications, there is also increasing recognition of the association between diabetes and other co-morbidities, including infections, depression, cognitive decline, reproductive abnormalities, notably Polycystic Ovarian Syndrome (PCOS), osteoporosis, sleep-disturbed breathing, and some subtypes of cancer [44]. The dual burden of diabetes and tuberculosis is particularly problematic for the SEA Region. The bi-directional association between depression and diabetes also increases the risk of noncompliance, hospitalisation, morbidity and mortality. These diabetes-related co-morbidities further add to the already escalating healthcare costs associated with diabetes in the region. Emerging data suggest that Asian populations may have different prevalences of some of these diabetes-related morbidities compared to Caucasian populations. For example, a recent meta-analysis including 33 studies has suggested that the cancer incidence is higher among Asian patients with diabetes compared to non-Asian populations [45].

A follow-up study from the CUPS in southern India has suggested an approximately 3-fold higher mortality among subjects with diabetes compared to control patients. When cause-specific mortality was examined, mortality due to cardiovascular complications and renal complications was increased in subjects with diabetes versus those without diabetes [46]. The prevalence of complications and related morbidities is set to increase further with the increasingly younger age of diagnosis noted in recent studies. With improved care and survival of individuals with cardiovascular and renal complications, it is envisaged that cancer will emerge as the leading cause of death among patients with diabetes, especially in Asian populations [44].

6. Prevention of diabetes

Prevention of diabetes and obesity are cost effective strategies. Several systematic clinical trials have shown the effectiveness and safety of lifestyle modification in preventing T2DM in varied ethnic populations [47]. Lifestyle intervention was found to be effective in Asian Indian subjects with IGT, with a risk reduction in incident diabetes of approximately 30% in 3 years compared with standard care [17]. The metabolic benefits were seen in non-obese subjects, independent of weight reduction. Ancillary benefits on cardiovascular risk factors were also observed. The extended Da Qing study in the Chinese population, who have biological characteristics similar to that of SEA populations, showed a 43% reduction in incidence of diabetes sustained for over 20 years [48].

The United Nations has urged its Member States to develop national strategies to combat the serious epidemic of diabetes. Among the SEA countries, India, Bangladesh and Sri Lanka have already initiated national programmes for better management, surveillance and prevention of diabetes [27].

7. The way forward

The challenges lie in improving the awareness level among the public on the risk factors for diabetes and then taking steps to prevent the disease. Empowering and educating self-care by patients and improving the training of medical community are also urgent requirements for countries in the SEA Region. Efforts to improve diabetes care and screening of complications have utilised different approaches. Several regional studies are examining the use of information technology such as mobile phone technology, internet-based healthcare management systems, and peer support networks in order

to improve patient empowerment and healthcare delivery [27,38]. The recent study by the authors in Chennai, India, in collaboration with researchers in the Imperial College, London, UK, showed that mobile phone messaging was an effective and scalable method to deliver advice and support towards lifestyle modification to prevent type 2 diabetes in men at high risk [49]. Implementation of diabetes prevention programmes and prevention of diabetic complications at a national level presents many challenges and requires a multi-faceted approach. Nevertheless, significant progress has been made through educating policy makers on the gravity of the situation, highlighting the lack of healthcare resources, the benefits of primary prevention, and through collaboration between ministries for health, education, agriculture and information. Population-based strategies to improve social and physical environmental contexts of healthy lifestyle pattern are essential for prevention of this major health hazard. Large scale and pragmatic intervention programmes to prevent complex diseases such as diabetes are expected to soon emerge due to the recent focus on preventive strategies.

8. Conclusions

SEA countries are facing a huge healthcare and economic burden from the rising prevalence of diabetes and its complications in both urban and rural communities. Adverse gene-environmental interactions due to rapid urbanisation and Westernisation have further escalated the prevalence of obesity and diabetes in most of these countries. The regional prevalence of diabetes among adults in SEA is estimated at 8.2% in 2013, which is projected to increase to 10.1% in 2035. The prevalence of IGT will rise from 2.8% to 3.2% in the same period. India has the highest number of people with diabetes in the Region. Wide heterogeneity exists among these countries in their social and economic attributes. Many of these countries have limited medical facilities. The poorest stratum of society faces the highest economic burden due to the disease, and also suffers from increased long-term complications and early mortality. There is an urgent need to create awareness about the non-communicable diseases among the public. National programmes should focus on prevention, early detection and control of these diseases.

Conflicts of interest

There are no conflicts of interest.

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