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REVIEW ARTICLE

Diabetes in developing countries

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Highlights

- Diabetes in developing countries is increasing and often undiagnosed. In South Asians, diabetes and related metabolic abnormalities develop at a younger age and at a lower body mass index and waist circumference than in Whites.
- Overall glycemic control and management of diabetes is suboptimal, driven by multiple factors (eg, unawareness, cost of drugs and insulin etc.), and the load of complications is high.
- To stem this epidemic, strong actions for prevention and management are required using innovative and low-cost approaches.

Abstract

There has been a rapid escalation of type 2 diabetes (T2D) in developing countries, with varied prevalence according to rural vs urban habitat and degree of urbanization. Some ethnic groups (eg, South Asians, other Asians, and Africans), develop diabetes a decade earlier and at a lower body mass index than Whites, have prominent abdominal obesity, and accelerated the conversion from prediabetes to diabetes. The burden of complications, both macro- and microvascular, is substantial, but also varies according to populations. The syndemics of diabetes with HIV or tuberculosis are prevalent in many developing countries and predispose to each other. Screening for diabetes in large populations living in diverse habitats may not be cost-effective, but targeted high-risk screening may have a place. The cost of diagnostic tests and scarcity of health manpower pose substantial hurdles in the diagnosis and monitoring of patients. Efforts for prevention remain rudimentary in most developing countries. The quality of care is largely poor; hence, a substantial number of patients do not achieve treatment goals. This is further amplified by a delay in seeking treatment, "fatalistic attitudes", high cost and non-availability of drugs and insulins. To counter these numerous challenges, a renewed political commitment and mandate for health promotion and disease prevention are urgently needed. Several low-cost innovative approaches have been trialed with encouraging outcomes, including training and deployment of non-medical allied health professionals and the use of mobile phones and telemedicine to deliver simple health messages for the prevention and management of T2D.

KEYWORDS

developing countries, diabetes, India, management of diabetes, prediabetes, prevention

1 | INTRODUCTION

Many developing countries have exhibited significant economic growth during the past decade, but current projections show a slowing of this trajectory.[1] Impressive and sustained economic growth has been seen in China, Brazil, and India, resulting in major urbanization, mechanization, and ingress of multinational food companies.[2,3] Increasing affluence has afforded the large middle socioeconomic stratum in these countries greater purchasing power for energy-dense "fast foods" and other processed food items.[3] This has resulted in major changes to physical activity and food choice behaviors, including changes from traditional eating patterns and cuisines. Such significant nutrition and lifestyle transitions have been strongly linked to the rapid escalation of obesity, metabolic syndrome, and type 2 diabetes (T2D).[2,4–6]

The prevalence of obesity has increased worldwide, and rapid increases have been seen in children, adolescents,[7] and adults,[8] exceeding 50% in men in some developing countries.[9] The increase in the number of people with diabetes each region from 2017 and 2045, and percent increase was highest in geographical regions that encompass developing countries, namely Africa (16 m, 41 m; 156%, respectively), Middle-East and North Africa (39 m, 82 m; 110%, respectively), South and East Asia (82 m, 151 m; 84%, respectively), and South and Central America (26 m, 42 m; 62%) compared with Europe, North America and the Western Pacific[10] (see Tables 1–2). Approximately 79% of adults with diabetes are living in low- and middle-income countries.[11]

Thus, the increase in diabetes in developing countries poses huge medicoeconomic problems to economies still being challenged by communicable diseases. Overall analysis of various aspects of diabetes, particularly syndemics with communicable diseases and gaps and innovation in prevention, diagnosis and clinical care, is needed.

2 | SEARCH STRATEGY AND OBJECTIVES

This is a narrative review of the literature, but the search strategy for relevant data on diabetes in each country followed a stepwise protocol.[12] For prevalence data, in the first stage an "Advanced" search of the online PubMed database, was conducted using the key words "diabetes mellitus" AND 'prevalence' AND "<country name>" to identify all relevant articles published up to June 30, 2018. The search terms were limited by language ("English"), species ("humans") and age ("all adults: 19+ years"). In the second stage, all articles identified in Stage 1 were screened for suitability for inclusion in the study by reading the article title and abstract. Inclusion criteria for Stage 2 were: prevalence study, data collection in given country, and biochemical measurements. The articles included were further screened for suitability during a third stage by reading the full text of the selected article. To obtain up-to-date prevalence data for individual countries, the studies that were most recent (after 2000), nationally representative, or with the largest sample size were included whenever possible. Studies with sample sizes less than 400 were excluded. For meaningful comparison of prevalence data among countries, unless stated otherwise age-standardized data are presented. In addition, other search terms were "developing countries", "low- and middle-income countries", "obesity", "prediabetes", "complications of diabetes", "management of diabetes", and "prevention of diabetes". To obtain additional data, websites of several diabetes-specific organizations were searched, including those of the International Diabetes Federation (IDF; https://www.idf.org/, accessed 22 March 2019), World Health Organization (WHO; http://www.who.int/diabetes/en/, accessed 22 March, 2019), American Diabetes Association (ADA; http://www.diabetes.org/, accessed 22 March, 2019), and the European Association for the Study of Diabetes (EASD; https://www.easd.org/, accessed 22 March, 2019). As a final step, manual searching was performed using the reference lists of selected articles. The top 10 countries with the highest number of adults with diabetes have been reproduced from the IDF Atlas[13] (Table 2).

This review is restricted to "type 2 diabetes mellitus", which will subsequently be described as "diabetes" throughout. The term "developing countries" has been used synonymously with "low- and middle-income" countries. Although we shall discuss several important issues, we would not discuss diabetes management in detail, and some other topics (eg, genetics[14–18]), which have been covered by others. It is important to note that although examples and statements refer to characteristics derived from data from a particular country, this information cannot always be generalized to all developing countries because they may differ in culture, diet, terrain, level of urbanization and health care systems. For detailed discussion and analysis of specific regions, readers are encouraged to access major reviews specific to country or region.[2,6,7,16,19–28] Overall, research outputs regarding all facets of diabetes remains poor in developing countries.[29]

3 | EPIDEMIOLOGY OF OBESITY AND T2D

As stated above, epidemiological data show a rising trend of obesity and diabetes in most developing countries. The prevalence of diabetes in individual developing countries is provided in Table 1, whereas trends in obesity and diabetes in selected countries or regions are described below. Worldwide, some 1.9 billion adults are overweight and 650 million are obese, according to Food and Agriculture Organization of the United Nations (FAO) data.[30] The situation is especially worrying in Latin America, where 96 million adults are obese.[31] A low prevalence of diabetes

TABLE 1 Prevalence of diabetes mellitus in developing countries

Country	Income category	Reference no.	Study year	Study setting	Sample size	Age group (y)	Prevalence of diabetes (%)			Diagnostic criteria
							All	Males	Females	
Afghanistan	L	55	2015	U	1129	25-70	9.9	9.8	10.1	WHO 2003, ADA 2003
Algeria	UM	56	2007	U and R	7656	≥20	14.2	20.4	10.7	WHO 1985
Angola	LM	57	2010	R	421	30-69	2.8	3.2	2.7	WHO/ASH 2003
Bangladesh	LM	58	2011	U and R	7541	≥35	9.7	9.3	10.4	WHO 2016, ADA 2005
Belize	UM	59	2003-06	N	2439	≥20	15.0	8.8	17.6	WHO 2001
Bhutan	LM	60	2005	U and R	2474	25–74	8.2	8.6	7.7	WHO 1997
Burkina Faso	L	61	2013	N	4417	25-64	5.8	6.3	5.4	WHO 2006
Cabo Verde	LM	62	2007	U and R	1762	15-64	12.7	NR	NR	WHO 2016, IDF 2015
Cameroon	LM	63	2000-17	P	37 147	24-54	5.8	6.8	6.7	WHO 2006
China	UM	64	2013	N	170 287	≥18	10.9	11.7	10.2	IDF 2015
Congo	L	65	2012-15	R	3936	≥15	2.8	NR	NR	WHO 2011
Costa Rica	UM	66	2010	N	3653	≥20	10.8	9.5	11.9	WHO 2004
Ecuador	UM	67	2010	N	2298	≥60	16.7	12.9	19.7	ADA 2017
Eritrea	L	68	2009	R	6265	25–74	5.0	8.3	4.3	WHO 2010
Ethiopia	L	69	2015	U and R	9141	15-69	3.2	3.5	3.0	WHO 2006
Gabon	UM	70	2012-14	R	2104	15-60	11.8	15.4	8.0	WHO 1995
Ghana	LM	71	2007-08	U and R	4089	≥50	3.9	1.7	2.2	WHO 2013
Grenada	UM	72	2008-09	N	2827	≥18	13.3	10.0	16	ADA 2008
Guatemala	UM	59	2003–06	NR	1397	≥20	9.6	10.4	8.8	WHO 2001
Guinea	L	73	2009	U and R	2491	15–64	3.5	3.3	3.7	WHO 2014
Haiti	L	74	2002-03	U	1545	≥20	NR	4.8	8.9	ADA 2005
India	LM	35	2008-15	U and R	57 117	≥20	7.3	NR	NR	WHO 2006
Indonesia	LM	75	2010	U and R	18 956	>18	5.6	NR	NR	WHO 1999, ADA 2013
Iraq	UM	76	2011-12	NR	5445	19-94	19.7	19.6	19.8	ADA 2010
Jamaica	UM	77	2007–08	N	2848	15-74	7.9	6.4	9.3	WHO 2006
Jordan	UM	78	2007	U and R	765	>18	19.5	17.9	20.7	WHO 2008
Kenya	LM	79	2009	R	1459	17-68	4.2	4.2	4.5	WHO 2000
Lebanon	UM	80	2008–09	U and R	2195	≥25	8.5	9.8	7.4	ADA 2014
Libya	L	81	2001	U and R	868	30-64	14.1	16.3	13	ADA 1997, WHO 1998
Macedonia	UM	82	2014	NR	NR	20–79	11.4	NR	NR	WHO 2005
Malawi	L	83	2009	N	3056	25–64	5.6	6.5	4.7	WHO 2005
Malaysia	UM	84	2015	U and R	19 935	≥18	17.5	16.7	18.3	WHO 2015
Maldives	UM	85	2004	U	1556	25–64	4.5	4.3	4.7	WHO 1999
Mauritius	UM	86	2015	U and R	265 000	20-74	22.8	22	23.5	WHO 1999
Mexico	UM	87	2006	U and R	6350	≥20	14.4	15.8	13.2	WHO 2006
Morocco	LM	88	2000	N	1662	≥20	6.6	6.6	6.6	ADA 1997
Mozambique		89	2005	U and R	2343	25–64	2.9	NR	NR	WHO1998
Myanmar	LM	90	2013-14	U and R	1372	25–74	NR	8.6	11.4	WHO 2006
Nauru	UM	91	2004	N	1592	15–64	13.7	13.0	14.4	IDF 2002
Nepal	L	92	2005-06	U and R	2006	≥30	NR	15.4	10.8	WHO 1998
Nigeria	LM	93	1990-2017	P	14 650	20-69	5.8	NR	NR	WHO 1999, ADA 2010
Pakistan	LM	94	2016-17	N	10 834	>20	26.3	NR	NR	WHO 2006, ADA 2016
Peru	UM	95	2010-12	N	1677	≥25	7.2	47.5	52.5	NR
Philippines	LM	96	2013–14	N	172 323	>20	5.4	5.6	5.3	NR
Romania	UM	97	2012–14	NR	2717	20–79	11.6	NR	NR	ADA 2012, WHO 2014
Russia	UM	98	2013-15	N	26 620	20–79	5.4	4.7	6.1	HbA1c ≥6.5%
Samoa	UM	99	2013	U and R	1622	25–64	24.3	27.0	22.6	WHO 2013, ADA 2009
Senegal	L	100	2009	U	600	≥20	17.9	NR	NR	WHO 2006
Sierra Leone's	L	62	2012–14	U	694	≥18	6.2	7.4	5.2	WHO 2006
South Africa	UM	101	2010	U and R	12 496	≥18	9.4	6.0	11.1	WHO 1999

TABLE 1 (Continued)

Country	Income category	Reference no.	Study year	Study setting	Sample size	Age group (y)	Prevalence of diabetes (%)			Diagnostic criteria
							All	Males	Females	
Sri Lanka	LM	102	2005–06	N	4485	≥18	10.3	9.8	10.9	WHO 1997
Sudan	LM	103	2015	U and R	5242	>18	18.7	20.3	17.6	ADA 2010
Suriname	UM	104	2013	U and R	3393	15-65	13.0	12.9	13.1	WHO 2012, IDF 2013
Thailand	UM	105	2012	N	16 903	>15	8.1	3.9	7.2	ADA 2009
Tonga	L	106	2012	N	2551	25–64	19.0	14.8	21.7	WHO 2012
Tunisia	LM	107	2005	N	7700	35-70	15.1	16.1	14.1	WHO 1999
Turkey	UM	108	2010	U and R	24 788	≥20	11.6	12.9	10.9	WHO 1999, ADA 2003
Uganda	L	109	2014	N	3689	18-69	1.4	1.6	1.1	WHO 2001
Venezuela	UM	110	2006-10	U and R	1334	≥20	8.0	11.0	7.0	ADA 2016
Vietnam	LM	111	2011-13	U and R	16 282	30–69	5.6	6.5	4.8	WHO 2006
Zambia	LM	101	2010	U and R	45 767	>18	2.9	2.7	3.0	WHO 1999

Abbreviations: ADA, American Diabetes Association; ASH, American Society of Hypertension; N, national; NR, not reported; P, pooled, WHO, World Health Organization; R, rural; U, urban.
This table includes countries that were selected from three income strata according to the World Bank classification in 2017 on the basis of gross national income (GNI) per capita:[112] low-income countries (L; n = 34), lower middle-income countries (LM; n = 46), and upper middle-income countries (UM; n = 56). For further data, please refer to International Diabetes Federation IDF) Atlas, 2017.[10]

TABLE 2 Top 10 developing countries according to the number of patients with diabetes (adapted from the International Diabetes Federation Atlas[13])

Country	No. diabetic patients ($\times 10^4$)
China	114 394.8
India	72 946.4
Brazil	12 465.8
Mexico	12 030.1
Indonesia	10 276.1
Russian Federation	8455.3
Egypt	8222.6
Pakistan	7474.0
Bangladesh	6926.3
Turkey	6694.5

was reported in Mexico in the 1960s, which had increased to 8.9% in adults in 2012, and is estimated to double every 10 years.[31] Projected rates in Mexico suggest that diabetes prevalence among adults (aged ≥ 20 years) may reach 13.7% to 22.5% by 2050, affecting 15 to 25 million individuals; this trend is seen concurrent with the rise of obesity.[32] The projected prevalence of obesity in 2050 is phenomenal for the Brazilian population: nearly 95% for males and 52% for females.[33] At the same time, cases of coronary heart disease, stroke, and diabetes are projected to at least double by 2050.[33] In northeastern China, from 2007 to 2013, there were age-standardized increases in the prevalence of obesity (from 16% to 19.4%, respectively) and related diseases (eg, diabetes: from 6.4% to 9.2%, respectively).[34] The prevalence of diabetes in China was less than 1% in 1980, but by 2013 this had increased to 10.9%.[16] Similar statistics of rapidly increasing rates of obesity and diabetes have been reported from India;[19,21,35–37] during past 15 years, countrywide prevalence has risen from 5.9%[38] to 7.3%.[35] The true burden of diabetes and its risk factors in Sub-Saharan Africa is difficult to ascertain due to the absence of high-quality data.[6] Although obesity in Sub-Saharan Africa appears to be a prime driver of diabetes and is generally increasing in urban areas, there is marked heterogeneity in prevalence, with northern and southern regions mostly higher than the global average, but central, eastern, and western regions lower than global averages.[28,39–41] Overall, the prevalence of diabetes is higher in urban areas in developing countries, with decreasing prevalence in semi-urban and rural areas.[21,42–46] However, some recent reports indicate that the prevalence of diabetes will increase in rural areas as well.[46,47] Importantly, a large percentage of patients in developing countries are undiagnosed.[10,26,48,49]

A limited number of studies on gestational diabetes mellitus (GDM), using diverse diagnostic criteria, are available from developing countries, most commonly from India, other South Asian countries, China, and a few from Africa and South America, and largely confined to urban areas.[50,51] The prevalence of GDM has varied according to diagnostic criteria and ranges from 0.4% to 24.3%, being particularly high in South Asia (13%-18%)[50] and China (9.3%-18.9%),[51] generally higher than that reported from developed countries. In a systematic review, it was noted that data from the African continent are scarce, and only six of 54 countries have been investigated,[52] showing marked variations in prevalence (0%-9%).[26] Overall, research, diagnosis, and clinical care of GDM in developing countries are inadequate.[53]

While looking at prevalence data, the following problems were discernible: the use of different diagnostic criteria for diabetes and varying age range, data collected from individuals from different areas of residence (rural vs urban), lack of nationally representative data, and variable methods of reporting prevalence (age specific vs gross prevalence). Some studies were conducted a long time ago, and

TABLE 3 Risk factors and determinants for type 2 diabetes in South Asians

Lifestyle and nutrition[6,21,24,113,123,131]
Diet: high intake of refined carbohydrate, sugars, trans fatty acids, and low fiber
Low level of physical activity
Poor cardiorespiratory fitness
Adverse *in utero* and perinatal nutrition[a]
Body composition[123,125,126,128,132–139]
High body fat for equivalent BMI in Caucasians
Excess abdominal adiposity, subcutaneous (deep subcutaneous), and intra-abdominal fat
Liver: excess fat (non-alcoholic fatty liver disease)
Pancreas: excess fat,[a] low β-cell reserve[a]
Less brown fat[a]
Skeletal muscle: low mass (sarcopenia)
Other factors:[a] vitamin D deficiency,[140,141] indoor[142] and outdoor[143] air pollution

Abbreviations: BMI, body mass index; NAFLD, non-alcoholic fatty liver disease.
[a]More research is required.

prevalence statistics may now be different. In addition, some details may have been missed when the full paper is not published in English.[54]

4 | DISTINCTIVE POINTS REGARDING DIABETES IN DEVELOPING COUNTRIES

Diabetes occurs a decade earlier in South Asians,[113–115] individuals from Asian countries,[116] and in Blacks in Sub-Saharan Africa.[117] A point of interest for prevention is the rapid conversion of prediabetes to diabetes.[113] Such early onset and faster progression to diabetes reinforces the potential value of early and aggressive intervention.[118,119] The body phenotype leading to diabetes is distinctive in some ethnic groups from developing countries, as detailed below (Table 3).

4.1 | "High body fat–low muscle mass–normal/slightly low body mass index" phenotype

In general, Chinese and Asians have lower height and weight, and a lower body mass index (BMI) than Whites.[16] They also manifest with a dysmetabolic state, multiple cardiovascular risk factors, and diabetes at a younger age and lower BMI and waist circumference than Whites and other races.[16,120–124] Propensity to develop diabetes at a lower BMI stems from the presence of greater insulin resistance and subclinical inflammation at younger ages than in other ethnic groups. The effect on insulin resistance could be contributed by truncal and abdominal subcutaneous adipose tissue, deep subcutaneous adipose tissue, intra-abdominal adipose tissue, and non-alcoholic fatty liver disease (NAFLD), as well as possibly high pancreatic fat content.[4,123,125,126] Because of these adverse body composition and metabolic attributes, different definitions of adiposity measures (BMI levels and waist circumference cut-off points lower than for Whites) have been advocated.[122,123,125,127–129]

Although body fat and location-specific fat depots are in excess, skeletal muscle mass is lower in South Asians, placing most of them in the "sarcopenia" category, which is independently associated with diabetes.[123,130] Overall, the phenotype of South Asians can be described as high body fat-low muscle mass-normal/slightly low BMI.[123]

5 | BURDEN OF COMPLICATIONS

5.1 | Microvascular complications

Poor awareness, a "fatalistic attitude", and consequent delayed diagnosis, inadequate treatment, and genetic predisposition are some reasons for the high burden of complications.[131] A high prevalence of nephropathy has also been reported, but figures vary (eg, the prevalence of microalbuminuria and proteinuria has been reported o range from 10% to 45%).[144] Further, rapid progression of renal dysfunction has been documented,[144] mostly because of poorly controlled glycemia and hypertension.[145] Interestingly, heightened ethnic susceptibility to develop nephropathy[146] and its faster progression[147] have been reported in South Asians compared with Whites. Similarly, those with African ancestry have an approximate 2-fold higher risk for end-stage renal disease,[148] and onset two decades earlier,[149] compared with Whites. The prevalence of peripheral neuropathy and peripheral vascular disease is high in developing countries. For example, in rural Ecuador, 24% of patients had peripheral arterial disease (PAD; as estimated by the ankle-brachial index) and 59% had neuropathy.[150] Although reliable population-based data are often unavailable, in general, the prevalence of retinopathy is higher in developing than developed countries.[151] Further, because of low awareness and often delayed diagnosis and infrequent visual examination and referrals to specialists,[6,152] many patients have already experienced vision-threatening retinopathy[153] or vision loss by the time they are screened.[154]

5.2 | Macrovascular complications

The mortality burden of cardiometabolic risk factors has shifted from high-income countries to low- and middle-income countries.[155] Many developing countries, particularly China and India, are witnessing a rapid increase in cardiovascular diseases. Among the prime drivers for increases in cardiometabolic disease in South Asians are unhealthy diets, hypertension, and diabetes[156] (Figure 1).

In addition, unhealthy diets contributed to cardiovascular-related mortality in 11 countries in the Middle East and North Africa in 2010.[157] The prevalence of coronary heart disease (CHD) varies according to country and diagnostic

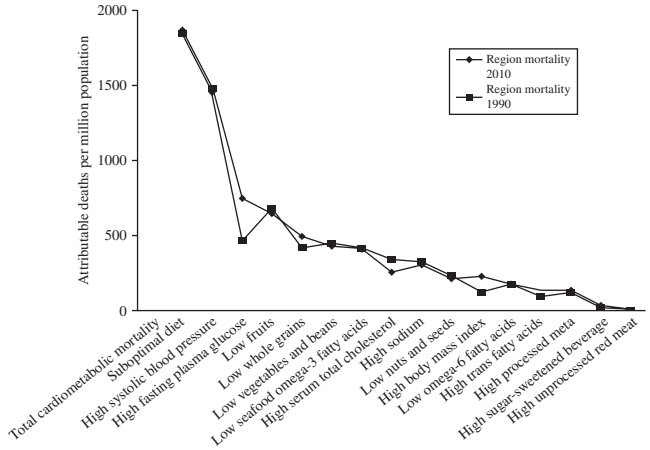

FIGURE 1 Mortality risks (per million adult population) from cardiometabolic causes attributable to dietary and metabolic risk factors, in India, Pakistan, Bangladesh, Nepal, and Bhutan in 1990 and 2010. Reproduced with permission from Yakoob et al[156]

criteria,[158] and has been recorded as the highest in South Asians.[158] Although data vary, there are some ethnic differences; CHD and PAD were less prevalent among African-Caribbeans[159] and CHD was more prevalent but PAD was less prevalent in South Asians[158] compared with Caucasians and Southeast Asian ethnic groups. However, recent data show increasing PAD in Sub-Saharan Africa.[160] Hypertension and stroke are common among African-Caribbeans.[6,159]

5.3 | Diabetic foot

Diabetic foot ulcers are the most problematic and resource-consuming complication of diabetes in developing nations. Although diabetic foot ulcers may not be as prevalent in some ethnic groups (eg, Asian Indians[158]), but associated complications (infections, osteomyelitis, or gangrene) are difficult to treat and may pose a risk for amputation and early mortality.[161,162] Diabetic foot ulcer may be triggered by the habit of walking barefoot, wearing improper footwear, unhygienic conditions, and rodent bites.[162–164]

6 | DETERMINANTS OF THE RAPID INCREASES IN DIABETES AND OBESITY IN DEVELOPING COUNTRIES

Although determinants are discussed below, a lifecycle of diabetes in developing countries with determinants and influencing factors is provided in Figure 2.

6.1 | Changing patterns of food consumption

Nutrition transition (ie, the consumption of refined grains, high saturated fat intake, increased consumption of sugar-sweetened beverages, and a low intake of fruits and vegetables) is a major cause of the increasing prevalence of obesity and diabetes in developing countries.[3,24,169–173] In general, these changes have arisen from a better economic status, falling prices for some foods, the emergence of new marketing channels, and the spread of supermarkets, freer trade and globalization of the food economy.[3,174,175]

6.2 | Urbanization, migration, and refugees

Increasing urbanization in many developing regions (Asia, Sub-Saharan Africa, South America) is linked to increasing diabetes due to mechanization and the "Westernization" of food habits, with other likely contributors being urban stress and pollution.[176,177] In addition, the influx of refugees from various developing countries to developed countries has increased. These individuals face stress, changing living conditions, and imbalanced diets. To date, such groups have not been researched adequately, but some data suggest increased risk of diabetes[178] and its coexistence with tuberculosis.[179]

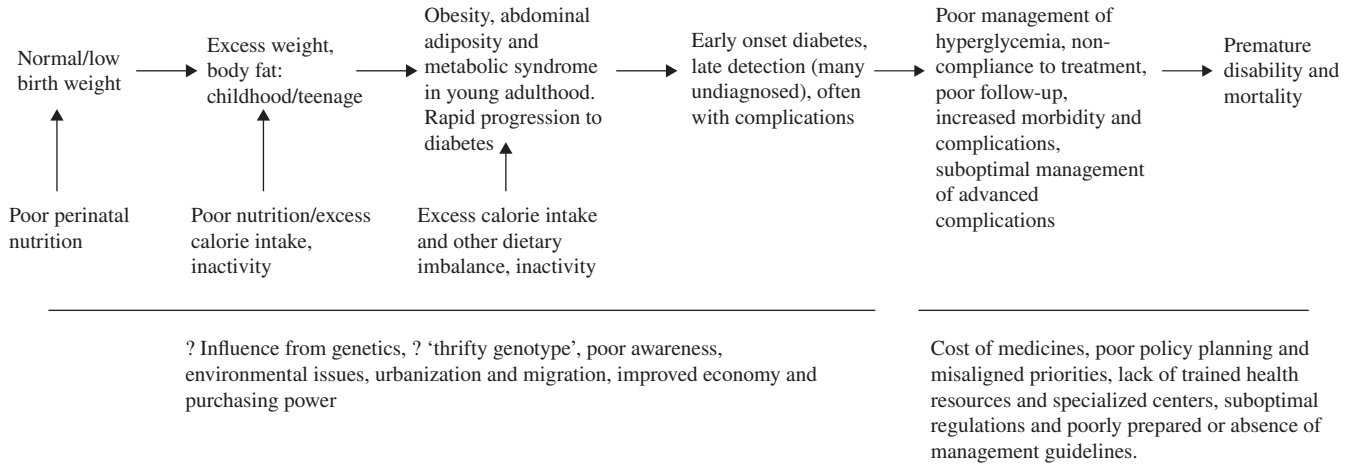

FIGURE 2 Determinants and influences on the development and course of diabetes during the lifecycle of individuals in developing countries (compiled from various sources[6,7,20,21,165–168])

6.3 | Physical inactivity

There is a paucity of data, but low levels of physical activity have been reported in developing countries.[20,180] In the Caribbean population, 90.5% of women and 59% of men do not accumulate enough activity to meet the WHO minimum recommendation.[181] Similarly, physical inactivity is prevalent in South Asia[118,123,125,180] and Latin America,[182] and has been shown to be related to abnormal glucose metabolism in China.[183] Such a lack of physical activity and sedentary behaviors is linked to mind set, urbanization and migration, mechanization, socioeconomic stratum, safety and weather concerns, and lack of open spaces and walking lanes.[125,184] Attempts have been made to formulate guidelines for physical activity (eg, in India[128,185,186]), but in most settings guidelines from developed countries are followed.[187]

6.4 | Poor awareness and access to prevention strategies

Awareness about diabetes and its risk factors is poor, more so in illiterate, transitioning, or rural-based populations,[24,188] posing a major roadblock for the prevention and management of diabetes.[189] Apart from poor awareness, correct nutrition, and lifestyle choices to prevent diabetes, other barriers to prevention strategies include difficulty in accessing health care, inadequate physician time to educate and screen for diabetes, and limited access to blood testing.[26,131,190,191]

6.5 | Perinatal undernutrition

Theoretically, linking perinatal undernutrition and increased rates of obesity in early childhood (increased feeding and excess intake of food) with diabetes and related diseases in later life is an attractive theory to explain increasing number of patients with diabetes in some segments of low-income populations of developing countries, but this requires further research.[192,193]

6.6 | Inconsistent or inadequate resources and low capability of healthcare systems to tackle diabetes and other non-communicable diseases

Importantly, despite increasing numbers of patients with diabetes and its complications (including other non-communicable diseases [NCDs]), the overall healthcare budget of developing countries is low[48] and focused on communicable diseases.[48] Various barriers exist in terms of the organization of health systems and care: ad hoc policies, insufficient human resources, poor availability and affordability of medicines, and poor support systems (eg, nutritionists, diabetes educators).[194,195] Interestingly, only 20 countries in Sub-Saharan Africa have operational action plan for diabetes,[6] leading to the conclusion that health systems are unprepared for the effective delivery of diabetes care in this region.[6]

The economic ramifications of the increased number of patients with diabetes are huge. Annual national direct costs of diabetes, borne mostly by patients, differ markedly between countries, ranging from US$3.5 billion to US$4.5 billion per annum in Africa between 2006 and 2016,[196] and US$31.9 billion in India in 2010.[197] Most of these costs relate to drugs, followed by diagnostic costs.[196,198] Expenditure increases significantly if a patient has associated complications of diabetes,[131,189,198,199] particularly stroke, a major coronary event, and amputation.[198–200] The highest burden due to the costs associated with diabetes was reported in individuals within the low-income group.[189,196]

7 | SYNDEMICS OF DIABETES WITH OTHER DISEASES

The concept of a syndemic refers to synergistic (often not directly associated with the index disease) health problems that affect the health of a population in the context of persistent social and economic inequalities.[201] Both HIV and tuberculosis are common in some African, South Asian, and South American countries,[48,131,201–205] and can contribute to insulin resistance and diabetes.[26,206] Conversely, the presence of diabetes increases the risk of tuberculosis.[206–208] The diabetes-tuberculosis association can lead to resistance to tuberculosis treatment,[209,210] the emergence of multidrug resistance,[211] and increased all-cause mortality.[212] Because of the escalation and convergence of diabetes and tuberculosis, bidirectional screening is advised[206,213] and has been shown to be successful in Mexico in a pilot study.[214] Such programs show a high prevalence (or incidence) of diabetes in tuberculosis patients.[215] Integrating a diabetes screening or control program within existing tuberculosis programs in these countries could be a useful plan going forward.[206,216]

8 | SCREENING FOR DIABETES

Screening for diabetes is an important point of discussion in view of the large number of undiagnosed patients in developing countries, but the process of screening at the population or national level must consider the wide disparity in prevalence rates within each country, as has been reported for India[217] and Sub-Saharan Africa.[6,48] In view of limited resources in most developing countries, mass screening for diabetes may be cost-intensive, and requires more research.[6] The authors of a recent systematic review and meta-analysis concluded that "screen and treat" policies alone are unlikely to have a positive effect on the diabetes epidemic.[218] In such a scenario, screening of high-risk populations using locally developed and validated algorithms could be a way forward.[219]

Interestingly, a microsimulation study on data from India suggested varying but substantial costs involved (between US $169 million and US$567 million) in large-scale community screenings using three questionnaire-based risk scores for Indians, and a high number of false positives.[220] Finally, the use of HbA1c without blood glucose data should be avoided for screening, as discussed below.[221,222]

9 | CHALLENGES IN DIAGNOSIS AND MONITORING

Although most urban areas may have facilities for blood glucose and HbA1c testing, there is continuing difficulty in getting even a blood glucose test in rural and remote areas of many developing countries.[48] The cost of HbA1c continues to be high but, even when available at lower cost, less than 20% of patients got this test done in Kenya[223] and India.[224] Further, because of the presence of anemia and hemoglobinopathies in many countries (India, Sub-Saharan Africa, China), the HbA1c values may be discordant with blood glucose concentrations, posing difficulties with diagnosis and monitoring.[221,222,225] Self-monitoring of blood glucose is poor, with the costs of the glucometer and testing strips being primary factors.[226]

TABLE 4 Roadblocks to the prevention and management of diabetes in developing countries

Prevention
Poor awareness and literacy
Policies and health care not focused on prevention (more on communicable diseases, treatment)
Shortage of and inadequately trained health manpower
Lack of guidelines for diet and exercise
Influence of audiovisual commercials for "energy-dense" foods
Near absence of school-based nutrition and exercise-related education and programs
Limited importance given by community to health prevention efforts (more focused on jobs, education etc.)
Management and rehabilitation
Cultural and social issues (eg, wrong beliefs, religious fasting, use of alternative medicines etc.)
Procrastination, "fatalistic attitude"
Late diagnosis and presentation with complications
Limited diabetes-related education (few diabetes educators)
Limited access to or use of HbA1c and self-monitoring of blood glucose; cost issues
Non-adherence to prescribed treatment
Inadequate availability of dugs and insulin; high cost
Syndemic fuelling of coexisting disease: with HIV, tuberculosis
Health system not prepared for adequate treatment and management
Poorly trained healthcare team for management and rehabilitation
Limited access to high-end management of complications (eg, diabetic foot)
Poor facilities for rehabilitation
Inconsistent regulations
Concerning standard of care, pharmaceuticals, taxation of unhealthy nutrients or oils, nutrition labeling
Lack of guidelines
Research
Poor output: most research studies have small sample sizes and are cross-sectional in design; few large-sample cohort studies
Basic research suboptimal

Compiled from various sources.[6,7,20,36,48,131,229,236]

10 | PREVENTION

Research regarding the prevention of diabetes and its complications in developing countries has shown encouraging results,[227] but data are scarce and mostly from India[228,229] and China.[230] Two long-term intervention studies from India[228] (30 months duration) and China[231] (6 years duration analyzed after 14 years) showed the benefits of intensive lifestyle interventions for prevention of diabetes. Other intervention trials for metabolic syndrome and obesity, predominantly in Asian Indians, also showed benefits of diet and lifestyle modifications.[118,229,232–234] Despite these studies and guiding principles, public efforts for prevention remain rudimentary in most developing countries because of various challenges[6,48,235] (Table 4).

11 | MANAGEMENT

11.1 | General approach

The quality of diabetes-related care in many developing countries is poor,[20,27,131,236] . Only a few countries in Asia and the Middle East (China, Thailand, Malaysia, the Philippines) have nationally representative data.[26,237] Glycemic control remains poor in developing countries;[26,27,188,238,239] for example, studies from countries in Asia, Latin America, and Africa have reported that more than 50% of patients did not achieve the HbA1c target.[131,188,239–241] This is contributed to by health system inadequacies (non-availability or cost of tests, including HbA1c, for public health, lack of medicines; see below), cost of treatment,[26] poorly trained doctors and paramedical staff,[24,131,191,241] a lack of diabetes educators,[191] and poor compliance with medications and follow-up.[20,48,131,242] At the same time, there is the recent emergence of highly specialized clinics and diabetes care centers in many countries to provide high-quality treatment.[243]

Increasing influence from social media regarding "fad" or "alternative diets"[244] and preferences for specific nutrients (eg, high carbohydrate diets in Asian countries, a traditional fondness for dietary sugar and oils high in saturated and trans fats in India)[3,24,125,245–251] and religious fasting (see below) may hinder the management of diabetes (Table 4). The approach to drug or insulin management is usually as per international guidelines, but should be further dictated by the phenotype of patients in developing countries.[232] For

example, lean patients with diabetes, as seen in many countries,[252,253] may be offered sulfonylureas and pioglitazone as preferred drugs.[254] In rural, underprivileged areas of developing countries, diabetes management protocols should be aimed at low-cost initial therapy with a sulfonylurea-metformin combination, and referral for further drug or insulin therapy to higher centers when glycemic targets are not met.[48,255] In those with obesity or a high body fat-insulin resistance phenotype (eg, south Asians), drugs directed towards weight loss should be preferred.[254,256] Further, there is a lack of information regarding prevention, dietary and medical interventions for GDM, maternal deaths due to diabetes, and postpartum diabetes[51] Management of GDM remains suboptimal in many settings.[53]

Morbidity and mortality due to hypoglycemia are important causes of concern due to poor health education, illiteracy, a lack of medical facilities, and intermittent or prolonged religious fasting.[131,257,258] Treatment of diabetic foot remains most challenging of all complications, particularly in underprivileged and rural-based populations, because of poor awareness, a lack of trained podiatrists, a delay in seeking treatment, and treatment expenses.[131,161–163] Scarcity of dialysis facilities,[24,259–261] specialists to perform photocoagulation,[262] and rehabilitation centers for stroke[131] hamper the management of those with advanced complications.

Finally, although many countries have diabetes care guidelines, these are poorly structured in terms of applicability, clarity, and socioeconomic contextualization.[263] In this context, it is important to note proposed guidelines for India stressing low-cost medications and insulins.[254] Equally important are diet and physical exercise guidelines, which are infrequently available in most developing countries.[185,264]

11.2 | Roadblocks to management

11.2.1 | Social and cultural issues

Low socioeconomic status (SES), place of residence, education, sex, level of awareness, poor nutrition, poor health behaviors (eg, tobacco use), a "fatalistic attitude", and self-care affect prevention, and can lead to poor compliance with treatment, poor control, and increased complications of diabetes in developing countries.[189,244,265–271] Inconsistencies regarding diets in the management of diabetes (eg, religious fasting[272,273] and traditionally held misconceptions[249,274]) hinder the achievement of proper glycemic control (Table 4).

11.2.2 | Availability, access, and cost of antihyperglycemic drugs and insulin

Barriers to accessing diabetes health care in developing countries include affordability, poor access to healthcare facilities and essential medicines, and a lack of sustainable financing and reliable supply systems[26,189,268,275–277] (Table 4). Patients with diabetes living in rural or remote areas, those with a low education level, and those with a low income or low SES have low access to diabetes medications, primarily due to inconsistent policies towards primary health care.[20,278] The increasing cost of insulin and medications, primarily borne by underserved populations, is an additional area of concern.[26,279–281]

11.2.3 | Use of complementary and alternative medicines

The use of complementary and alternative medicines (CAMs) in the treatment of diabetes is prevalent in developing countries,[282,283] often driven by the belief that these are without adverse effects and are inexpensive (Table 4). Given their low cost and the prevalent belief that they have no side effects, CAMs may be used as the sole therapy for diabetes, and may therefore cause potential harm.[131,284,285] The efficacy and safety of CAMs remain doubtful given sparse and methodologically weak studies.[286] Yoga has beneficial effects on glycemic control compared with physical exercise in T2D, but individual studies showed considerable heterogeneity; hence, firm conclusions cannot be made.[287]

12 | APPROACH TO TACKLING DIABETES AND OTHER NCDs IN DEVELOPING COUNTRIES

Various approaches have been suggested to tackle diabetes and other NCDs in developing countries,[20,48] but in the following para we shall discuss some key areas and low-cost innovative approaches.

12.1 | Health system reforms

Reform of health systems in developing countries can occur in the following areas: building political commitment and addressing health system constraints, developing public policies in health promotion and disease prevention, creating new service delivery models and ensuring equity in access and payments,[288] and having consistent guidelines for the prevention and management of diabetes.[20,236] Having stated this, the WHO package of essential non-communicable disease interventions for primary health care in low-resource settings, which aims to bridge the gap in diabetes care between rural and urban areas and strengthen care at the secondary and tertiary levels, has been advocated[289] but remains to be tested and applied widely.

12.2 | Appropriate and innovative healthcare approaches

12.2.1 | Task shifting

It has also been emphasized that factors that facilitate effective diabetes care and management should include innovative care models and "task shifting".[290] Task shifting (provision of basic care; eg, provision of advice and medications by paramedical workers other than physicians) could

TABLE 5 Innovative and low-cost approaches for the prevention and management of diabetes in developing countries

Task shifting: diabetes care delivered by pharmacists, nurses and other trained non-medical individuals
School-based intervention programs for nutrition and obesity
Health promotion using mobile phones or digital platforms (mHealth)
Screening and care of diabetes-related eye problems using mobile vans, teleophthalmology and using smartphones[a]
Diabetes diagnosis and care at doorsteps using mobile vans[a]
Bidirectional screening of tuberculosis (also HIV) and diabetes (integration of diabetes control in communicable diseases program)
Interventions to improve perinatal nutrition (integration with NCD program)
Culturally appropriate community engagements
Lifestyle intervention at workplaces
Taxation on unhealthy foods and oils[a]
Universal health insurance[a]

Abbreviations: NCD, non-communicable disease.
[a]Remain to be tested widely.

provide care in areas with a scarcity of physicians (Table 5). A randomized intervention trial using non-physician care coordinators and decision support with electronic health records in resource-challenged clinics in India and Pakistan showed improvements in lipids, blood pressure, and HbA1c levels.[291] Overall, based on an analysis of data from 20 developing countries, lifestyle education led by allied health professionals may be as effective as that led by physicians for the prevention and management of diabetes.[292]

12.2.2 | mHealth

Population-level effects of mHealth applications (eg, multimedia and short message service [SMS] texting) is being realized in the context of diabetes and other NCDs. Mobile phone messaging appears to be an effective and acceptable method for lifestyle modification and the prevention of diabetes,[293] improving medication adherence and HbA1c, and self-monitoring of blood glucose[294,295] and other diabetes-related behaviours.[293,296,297] Mobile diabetic retinopathy screening and treatment models can be readily replicated for remote or rural areas in developing countries[298] and are cost-effective,[299] but need long-term research.[300]

12.2.3 | Mobile health care at doorsteps

The cost of commuting and waiting in hospitals precludes many underprivileged people from seeking adequate care; in such cases, diabetes-related healthcare could be delivered at the doorstep of the underserved population (Figure 3, Table 5).[302] A McKinsey report has also noted that the mobile van program could be broadened to include structured referrals and counseling for patients with diabetes.[303]

12.2.4 | Nutrition and lifestyle interventions in pregnancy, early childhood, and adolescence

Balanced nutrition starting before pregnancy and then through pregnancy and the neonatal period for the prevention of childhood and adolescent obesity (lifecycle approach)

FIGURE 3 Diabetes care at doorsteps using customized mobile vans [project funded by the World Diabetes Foundation[301]). A, A dummy patient undergoing electrocardiogram examination inside a customized mobile diabetes vehicle in Trilokpuri, East Delhi, North India. The fundus photograph, was obtained using a 3nethra fundus camera, Forus Health Technologies, California, is seen on the laptop screen to the left of the patient. This fundus photograph will be sent to a tertiary care center using Skype for expert advice. B, A diabetes health camp in Mangolpuri, West Delhi, North India, for the underprivileged population. A customized mobile diabetes vehicle, the interior of which is shown in A (in Hindi "*Diabetes Rath*"), is seen in the background

has been reported to improve metabolic status and may prevent the onset of diabetes.[166,304,305] Although trials from the perinatal period are scarce, lifestyle management of childhood obesity appears to be effective in improving anthropometric and metabolic parameters and β-cell function.[7,306–311] Interventions for the prevention of GDM are few, but have shown encouraging results in China[312] and India.[313] In view of poor nutrition before, during, and after pregnancy being a possible factor in the causation of diabetes and other NCDs, integration of NCD prevention in child and health programs is a promising idea[314] that needs more research.

12.2.5 | Culturally appropriate community engagement

Tailoring interventions across language, location, and messaging can be effective in improving risk factors for progression to diabetes.[315] Interventions with culturally tailored modules can significantly improve HbA1c and fasting blood

glucose, and result in weight loss.[315] Culturally and linguistically appropriate health education messages in face-to-face individual and group sessions including demonstrations of model meals and cooking techniques were shown to be successful in improving blood glucose, blood pressure, and knowledge regarding diabetes of rural participants in south India.[316] Use of mass communication methods improved the composite score for chronic disease and risk factor knowledge and attitude among urban and rural-based women in India.[317] Clearly, more research is needed regarding effective messages for the prevention and control of diabetes tailored to geographical and cultural contexts in South Asia.

12.2.6 | Strategies using legal framework or governmental actions, including taxation

There is increasing realization that upstream actions like legal regulations may also help in the prevention of diabetes. Using consumption and price variations data from a nationally representative survey of 100 855 households in India, Basu et al.[318] showed that a 20% tax on sugar-sweetened beverages (SSBs) could reduce the prevalence of overweight and obesity, as well as the incidence of T2D. Mexico introduced an SSB tax in 2014 and projected that a 10% reduction in SSB consumption with 39% calorie compensation among Mexican adults would result in a decrease in incident cases of T2D, stroke, myocardial infarctions, and fewer deaths.[319] However, such a taxation-induced effect on obesity could be temporary, and SSBs could be substituted with similar, but lower-cost beverages. Overall, a high tax rate on sales of SSBs[320] or a reduction in sugar content[321] could be effective in reducing obesity and diabetes.

13 | CONCLUSIONS

The burden of T2D and its complications is substantial and escalating, and poses a huge economic burden. Major challenges include unawareness, undiagnosed cases, coexistence of T2D with tuberculosis and other infections, the high cost of diagnostic tests, insulin, and drugs, and the scarcity of trained health workers. Efforts to contain this epidemic should include increasing awareness, effective primary prevention, the use of allied health professionals for prevention and education, improving the standard of care, using mobile phones and telemedicine to deliver health messages, and regulation to promote healthy foods and curb unhealthy oils and SSBs.

DISCLOSURE

AM is a consultant to Abbot, Wockhard, Eli Lilly, Sanofi, Boehringer, Astra Zeneca, Janssen, Dr Reddys Lab., Novartis, Lupin, Azzka, Roche, Cipla, and Serdia. The other authors have no conflicts of interest to disclose.

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