New insights on diabetes mellitus and obesity in Africa–Part 1: prevalence, pathogenesis and comorbidities

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ABSTRACT
Evidence continues to accumulate on the rising burden of diabetes mellitus at a higher pace in Africa. In a series of two papers, we sought to summarise recent evidence on diabetes and obesity in Africa based on a systematic review of studies published between January 2002 and October 2012. This first paper on the prevalence, pathogenesis and comorbidities shows that the increase in diabetes prevalence has paralleled that of obesity in Africa. Recent surveys on diabetes and obesity have been largely suboptimal. Hence, the need for more representative and robust continent-wide prevalence figures, which may be somehow achieved through pooling of existing data. Prospective studies linking environmental risk factors to disease occurrence and outcomes remain scarce, and genetic factors for diabetes or obesity have not been extensively assessed. The health consequences of diabetes are manifold, and include a complex interaction with other conditions like HIV infection and sickle cell disease/trait.

INTRODUCTION
The importance of diabetes mellitus as a major threat to the health of populations in Africa is increasingly being recognised, partly as the result of the growing global interest for chronic diseases in general, but also of the increasing availability of evidence to support the case of diabetes in Africa.[1] Estimates from the International Diabetes Federation (IDF) for the year 2012 indicate that people with diabetes comprise about 371 million individuals.[2] About 7.5% (27.5 million) of this population reside in Africa including 14.7 million in sub-Saharan Africa (SSA) and 12.8 million in North Africa and Sudan. IDF's projections suggest that the global number of people with diabetes will increase by 51% to 552 million by 2030. The largest expected relative growth will occur in Africa, which by then will be home to about 49.7 million people with diabetes (81% relative increase), translating into about 9% of the global population with diabetes.[2]

The rapid increase in diabetes figures in Africa is largely attributed to accelerated environmental changes characterised by rapid urbanisation and modernisation, as well as ageing of the population. The underlying diabetes-promoting behavioural changes include the adoption of sedentary lifestyles and unhealthy eating habits. Together with the ensuing overweight and obesity, these result in many people developing diabetes and other risk factors for cardiovascular diseases. Globally, overweight and obesity have been recognised as the main drivers of the growing epidemic of diabetes. Between 1980 and 2008, the body mass index (BMI) of the adult population in the world increased by about 0.4 kg/m^2 per 10 years in men and 0.5 kg/m^2 in women.[3] During this same time interval, the rates of change in BMI in men and women across SSA and North Africa were always higher than the global average.[3] The average glucose levels of the population in Africa have mostly remained low within this period, likely reflecting the time lag needed before the increasing BMI can have a sizable effect on the prevalence of diabetes mellitus.[4]

In this series of two papers, we provide a critical review of recent evidence pertaining to diabetes mellitus (type 2 diabetes in particular) and obesity in Africa. More than a simple update of existing reviews that have addressed the subject matters from a SSA or a Northern African perspective,[5–7] we use a broader African perspective to summarise recently published evidence. Where relevant, we contrast the evidence by region, and identify the research gaps, remaining challenges, and existing opportunities to improve diabetes and obesity prevention and control in Africa. The first article of the series focuses on the prevalence, pathogenesis and comorbidities of obesity and diabetes, using the most relevant evidence published over the last 10 years. The sources of the evidence and approaches for gathering them are presented in detail in the second paper.[8]

PREVALENCE AND INCIDENCE OF DIABETES AND OBESITY
Prevalence studies of diabetes
A total of 13 community-based prevalence studies have been published over the last 10 years from nine SSA countries and Tunisia (table 1). The overall prevalence of diabetes (age-standardised only in two studies[9][10]) ranged from 2.8% in rural Angola[11] to 28.2% among urban mixed-ancestry South Africans.[9] The proportion of screen-detected cases (reported in five studies) among those with diabetes ranged from 21.3% in rural Congo (Democratic Republic) to 90% in urban Senegal.[12] Sex-specific prevalence was reported in seven studies, showing higher rates in men than women in three studies[11][13][14] and the reverse in four others.[10][12][15][16] Two studies provided urban versus rural comparisons in the same countries, both showing urban prevalence of diabetes about twice that observed in rural settings.[17][18] Three of the studies used self-selected sample of participants,[15][19][20] two studies from South Africa[9][10] and one from Angola[11] used oral glucose tolerance

Table 1 Selected population-based prevalence studies on diabetes in Africa, 2002–2012

Study	Country	Sample	Sampling	Setting	Age (years)	Diagnosis	Prevalence of diabetes (%)			
							Overall	Men	Women	Undiagnosed
Evaristo-Neto[11]	Angola	421	Random	Rural	30–69	OGTT	2.8	3.2	2.7	–
Echouffo-Tcheugui[15]	Cameroon	1591	Self-selected	Urban	43.7	FBG	15.3	13.7	17.0	6.3
Katchunga[17]	DRC	424	Random	Urban	53.3	RBG	4.7	–	–	1.0
Katchunga[17]	DRC	245	Random	Rural	58.5	RBG	2.9	–	–	1.6
Ploubidis[18]	Kenya	2959	Random	Rural	64.7	RBG	5.1	–	–	–
Ploubidis[18]	Kenya	1437	Random	Urban	60.8	RBG	10.1	–	–	–
Ejim[13]	Nigeria	858	Random	Rural	59.8	FBG	4.4	7.3	3.3	–
Duboz[12]	Senegal	600	Random	Urban	>20	FBG	17.9	14.0	21.8	16.2
Peer[10]	South Africa	1099	Random	Urban	43.3	OGTT	12.1 (13.1)	10.2 (11.3)	13.8 (14.7)	4.9
Erasmus[9]	South Africa	642	Random	Urban	50.9	OGTT	28.2 (26.3)			18.1
Baragou[16]	Togo	2000	Random	Urban	39	2 FBG	7.3	6.9	7.3	–
Nsakashalo-Senkwe[54]	Zambia	1928	Random	Urban	≥25	FBG	2.7	–	–	–
Hammami[14]	Tunisia	598	Random	Urban and rural	72.3	RBG	27.4	29.2	26.5	–
Chamie[20]	Uganda	2283	Self-selected	Urban	35	RBG	3.5	–	–	0.8

Figures within parenthesis are age-adjusted.
FBG, fasting blood glucose; OGTT, oral glucose tolerance test; RBG, random blood glucose.

test to diagnose diabetes, while the remaining used random or fasting capillary glucose measurement (table 1).

In general, the quality of the available prevalence studies of diabetes remains suboptimal, such that in many settings these studies do not provide accurate estimates of the magnitude of the condition. Over the last 10 years, several African countries have made significant progress by embracing the WHO STEPwise approach to chronic disease surveillance (STEPS), which involves repeated population-based data collection on the levels of risk factors.[21] At least 20 countries in Africa have conducted one such survey.[22] Some surveys have collected data to assess diabetes status, usually based on self-reports and fasting capillary glucose in a subsample of the surveyed population. Very few of the STEPS survey data have been appropriately analysed and published to allow regional comparisons.[22] However, these surveys used similar methodological approaches to sampling and data collection, which offers an opportunity for refining and updating prevalence data for diabetes and other risk factors, through pooling of individual countries' data to generate more reliable regional and continent-wide figures. Such an approach has been used for instance for physical activity.[22] Making the existing STEPS data publicly available may foster collaboration within Africa and beyond to maximise its exploitation.

Studies of incident diabetes and risk factors
Risk factors for diabetes in Africa have been investigated mostly using the cross-sectional design, which has the limitation of not establishing the sequence of events.[6] A recent overview of longitudinal studies conducted in SSA,[23] with relevance to cardiovascular disease and diabetes, showed that the few available prospective studies found the main determinants of incident diabetes to be baseline glucose tolerance status and BMI.[23] In a more recent cohort study among people aged >65 years in Nigeria, urban residence and high socioeconomic status were found to be the main risk factors of self-reported incident diabetes.[24] A few cohort studies are currently underway in Africa; these include the Prospective Urban Rural Epidemiology Study (African sites)[25] and the Bellville-South cohort in South Africa.[9] Preliminary data from the Bellville-South cohort show rates of abnormal glucose tolerance to be very high among

mixed-ancestry populations, and determined essentially by the baseline cardiometabolic risk profile.[26]

Prevalence studies of obesity
About 20 prevalence studies on obesity in African populations were published over the last decade, with nearly half of them originating from Nigeria (table 2). The age bracket of the included population suggests an increasing interest for childhood and adolescent obesity in Africa, with over half of the studies conducted in the paediatric population. Childhood obesity on its own is a broad and complex topic and is not discussed further in the current review. Available studies are also characterised by a low representation of rural populations. These studies have reported prevalence figures for obesity in adults ranging from 5% in rural Uganda[27] to 30% in Rural Nigeria.[13] The frequency of obesity is almost always higher in female subjects than in male subjects (table 2). When reported, the prevalence of overweight across studies was most often higher than that for obesity, with differentially higher figures for women in some studies, but not all. Very few studies reported the prevalence of abdominal obesity, which ranged from 7.5%[28] to 66.5%[29] among adults in urban Nigeria. There was no North-Africa versus SSA pattern in the profile of published studies, partly due to the small number of studies from Northern Africa. Cross-sectional surveys that used WHO STEPS approach have also reported a variable crude prevalence of obesity ranging from 2.2% in a nationwide survey in Madagascar to 25.1% in Seychelles.

PATHOGENESIS OF DIABETES AND ROLE OF OBESITY
The increase in the prevalence of type 2 diabetes appears to be closely linked to the upsurge in obesity in Africa. While the role of obesity in the pathogenesis through insulin resistance is not disputed, the relative contributions of insulin resistance and β-cell dysfunction to the pathophysiology of type 2 diabetes in African populations are not completely clear. Data on the changes in the β-cell function and insulin resistance in the early stages of the disease process in African populations are scarce.[30] Although there is accumulating evidence to indicate that the pathogenic processes in type 2 diabetes are triggered by environmental factors, namely, physical inactivity and dietary changes, which mainly exacerbate insulin resistance, the genetic basis for

Table 2 Population-based prevalence studies on overweight and obesity in Africa

Study	Country	Sample	Sampling	Setting	Age (years)	Obesity (%)			Overweight (%)			Abdominal obesity (%)		
						Overall	Men	Women	Overall	Men	Women	Overall	Men	Women
Fouda[55]	Cameroon	552	Random	Urban	34.5	23.4	17.8	36.1	49.1	51.7	43.2	35.2	19.8	69.8
Sani[56]	Nigeria	300	Convenient	Urban	37.6	21.3	10.9	29.2	32	–	–	43.7	12.4	67.3
Ejike[28]	Nigeria	1584	Random	Urban	21.8	1.3	0.4	2.5	19.4	17.1	22.3	7.5	1.3	16.1
Ejim[13]	Nigeria	858	Random	Rural	59.8	30	21.1	33.6	–	–	–	31	2.4	42.6
Wahab[57]	Nigeria	300	Convenient	Urban	–	21	9.3	29.8	53.3	41.9	62	–	–	–
Okafor[29]	Nigeria	898	Random	Urban	48.7	21.2	–	–	40.4	–	–	66.5	–	–
Mkhonto[58]	South Africa	532	Convenient	Rural	45.9	24.4	9.6	29.6	26.1	17.7	29.0	–	–	–
Malaza[41]	South Africa	14 198	Convenient	Rural	≥15	45.7	15.9	45.7	23.3	31.3	4.9	–	–	–
Baragou[16]	Togo	2000	Random	Urban	39	25.2	16.7	32.2	–	–	–	–	–	–
Mayega[27]	Uganda	1656	Random	Rural	44	5.3	2.2	8.2	12.3	7.5	16.9	13.8	1.4	24.5
Rudatsikira[59]	Zambia	1928	Random	Urban	–	14.3	5.1	18.6	–	–	–	–	–	–

insulin resistance and β-cell dysfunction has not been widely investigated in African populations. While environmental factors are very important, genetic factors probably have a role. Some of the diabetes genes discovered through genome-wide association studies elsewhere have recently been confirmed in African populations. However, this has been restricted to a smaller number of genes loci studied among West African populations from Nigeria and Ghana,[31] and Northern African populations from Tunisia and Morocco.[32–35] Although some of the studies on diabetes have also investigated obesity, overall, studies of the genetics of obesity in African populations remain rare.[36–38] Given the significant interethnic differences in risk allele frequency and location in studies conducted out of the continent, it is logical to speculate that there may be some specificities of African populations, especially given the potential variability that may exist from the North to South of the continent.

CONCURRENT AND COMORBIDITIES OF DIABETES IN AFRICA
Diabetes, obesity and HIV infection
There is increasing evidence linking HIV infection with diabetes mellitus and impaired glucose tolerance, resulting from the natural history of HIV infection, comorbidities and treatments.[39 40] The improved survival among people with HIV in Africa, following the improved access to highly active antiretroviral therapy (HAART) and treatment of comorbidities in many countries in the region in the recent years, will likely affect the prevalence of diabetes and dysglycaemia in Africa. However, the true magnitude of these effects is yet to be determined, and the mechanisms involved still to be investigated.[39]

There have been suggestions that the burden of HIV infection could mask the emerging epidemic of obesity in Africa,[39] due to HIV related weight loss and wasting. Although access to HAART has significantly increased in SSA in recent years, population-based measures of effects, if any, on the occurrence of obesity have been lacking. In a cross-sectional study conducted in 2010 on a large sample from rural South Africa, with a high prevalence of HIV infection (24.1%), HIV infection was still associated with low BMI, even in the context of high access to HAART.[41] In this study, while the prevalence of overweight was not different by HIV status, obesity was significantly more prevalent among HIV-negative individuals than HIV-positive participants (24.5% vs 20.0%). Being on HAART was associated with low BMI, a finding difficult to interpret in the absence of adjustment for the severity of HIV infection and the duration on HAART.[41] Furthermore, whether some of the observed

effects could be ascribed to the fact that HIV patients on HAART are more likely to be health conscious than untreated patients or HIV negative remains unknown.

Diabetes and SCD
A recent study from Cameroon has provided findings suggesting similar frequencies of sickle cell trait (SCT) in people with diabetes and in the general population,[42] and that the presence of SCT did not affect the metabolic control of diabetes. A striking fact in this study, however, was the older age of patients with SCT, for a comparable duration of diagnosed diabetes with the non-trait patients, indicating a possible late onset of type 2 diabetes in SCT carriers. Clarifying a possible link between SCT and diabetes onset or early attrition in diabetes is important in Africa, where the largest number of people with SCT and sickle cell disease (SCD) are found. The growing population with diabetes in Africa will likely include more people with both diabetes and SCT/SCD, and may result in differential features of diabetes across the continent, since the majority of those with SCT/SCD are typically found in Equatorial Africa, the epicentre of the disease.[42] Resolving this uncertainty may invite efforts beyond what a single country can achieve. The health consequences of the co-occurrence of diabetes and SCT on the outcomes of both conditions are yet to be clarified.

Diabetes and MetS
Early studies of cardiovascular risk in people with diabetes were based on single risk factor approach.[43 44] In recent studies, investigators have increasingly embraced the multiple risk factors approach to cardiovascular risk evaluation in diabetes. About 13 such studies published over the last 10 years from six SSA and one Northern Africa countries have characterised the cardiovascular disease risk in diabetes in clinical setting through screening for metabolic syndrome (MetS, table 3). These studies have used various criteria to define MetS, which makes comparison across studies difficult, but studies have been consistent in showing higher prevalence of MetS in women with diabetes than in men. Among the studies that used the IDF criteria to diagnose MetS, the prevalence ranged from 27.1% in urban Congo (Democratic Republic)[45] to >80% in a nationwide sample in Seychelles.[46] The variable prevalence across studies is mostly due to the use of variable thresholds, not supported by local evidence, to screen for different components of MetS. This is reflected by the non-perfect agreement between diagnostic criteria in those studies that have compared the yield of different criteria in the same population in Africa.[46–48]

Table 3 Studies of metabolic syndrome in diabetes in hospital settings across Africa

Study	Country	Year published	Sample	Setting	Age	Duration	Criteria	Metabolic syndrome (%)		
								Overall	Men	Women
Longo-Mbenza[45]	DRC	2010	1266	Urban	50	–	IDF	27.1	–	–
Kengne[47]	Cameroon	2012	308	Urban	55.8	3.0	IDF	71.7	58	86.1
	Cameroon	2012	308	Urban	55.8	3.0	NCEP	60.4	42.7	78.8
Alshkri[60]	Libya	2008	99	Urban	56	9.4	NCEP	92	82	97
	Libya	2008	99	Urban	56	9.4	IDF	81	68	88
	Libya	2008	99	Urban	56	9.4	NCEP	60.4	42.7	78.8
Ogbera[50]	Nigeria	2010	973	Urban	58.6	6.9	JIS	86	83	87
Unadike[61]	Nigeria	2009	240	Urban	50.8	–	NCEP	62.5	41.5	79.1
Adediran[62]	Nigeria	2007	408	Urban	56	–	WHO	51	44	56
Isezuo[63]	Nigeria	2005	254	Urban	52	6.1	WHO	59	–	–
Alebiosu[64]	Nigeria	2004	218	Urban	53.4	8.5	WHO	25.2	25	25.6
Puepet[65]	Nigeria	2009	634	Urban	54.2	–	IDF	63.6	74.5	54.9
Kelliny[46]	Seychelles	2008	130	Nationwide	25–64	–	NCEP	–	66.8	87.1
	Seychelles	2008	130	Nationwide	25–64	–	WHO	–	85.5	79.7
	Seychelles	2008	130	Nationwide	25–64	–	IDF	–	74	93
Kalk[66]	South Africa (black)	2008	500	Urban	48.3	2.0	IDF	50.2	46.5	74.1
	South Africa (white)	2008	254	Urban	54.1	6.0	IDF	73.6	52.9	73.1
Makuyana[67]	Zimbabwe	2004	109	Urban	–	–	WHO	43	–	–

IDF, International Diabetes Federation; JIS, Joint Interim Statement; NCEP, National Cholesterol Education Program, Adult Treatment Panel III.

The Joint Interim Statement (JIS) criteria recently published as part of the efforts to harmonise the definition criteria for MetS has not been recommended for use in people with diabetes as virtually all those with diabetes would qualify for MetS based on the JIS criteria.[49] Studies of MetS in people with diabetes in Africa using the JIS criteria have rather found variable prevalence rates not reaching 100% in all circumstances.[47 50]

HEALTH CONSEQUENCES OF DIABETES
The burden and likely determinants of the well characterised microvascular and macrovascular complications of diabetes, and related morbidity and mortality in Africa have been recently described.[6 23 39 43 51 52] Recent global efforts have focused on establishing a connection among diabetes mellitus, treatment and cancer risk. This issue was recently examined in a cohort of 9559 participants followed for a median of 15.1 years in Mauritius.[53] The study revealed a high risk of all-cause cancer mortality with increasing 2-h baseline glucose in men, but not in women. In an analysis stratified by gender and ethnicity, a significant association between baseline diabetes and all-cause cancer mortality was found only among South Asian men.[53] Although this study suggested that the increasingly reported association between diabetes and cancer risk may also apply to populations in Africa, the study was statistically underpowered to provide a definitive answer to the question in this setting.

CONCLUSIONS
Diabetes mellitus and obesity are important health challenges faced by countries in Africa, which are currently experiencing rapid transitions. Despite the uncertainties about the true magnitude of the conditions, diabetes and obesity figures will increase in Africa over the next few decades at a faster pace than elsewhere in the world. There is a hope that our knowledge base on the burden of diabetes and obesity in Africa can be substantially improved at little additional cost through careful exploitation of data already collected in many countries in recent years. However, new research is ultimately needed to

better characterise the interaction of genetic and environmental factors on the occurrence of diabetes and obesity in Africa.

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