A Multiethnic Study of Pre-Diabetes and Diabetes in LMIC

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ABSTRACT

Background: Diabetes mellitus is one of the leading causes of death and disability worldwide. Approximately three-quarters of people with diabetes live in low- and middle-income countries, and these countries are projected to experience the greatest increase in diabetes burden.

Objectives: We sought to compare the prevalence, awareness, treatment, and control of diabetes in 3 urban and periurban regions: the Southern Cone of Latin America and Peru, South Asia, and South Africa. In addition, we examined the relationship between diabetes and pre-diabetes with known cardiovascular and metabolic risk factors.

Methods: A total of 26,680 participants (mean age, 47.7 ± 14.0 years; 45.9% male) were enrolled in 4 sites (Southern Cone of Latin America = 7,524; Peru = 3,601; South Asia = 11,907; South Africa = 1,099). Detailed demographic, anthropometric, and biochemical data were collected. Diabetes and pre-diabetes were defined as a fasting plasma glucose ≥126 mg/dl and 100 to 125 mg/dl, respectively. Diabetes control was defined as fasting plasma glucose <130 mg/dl.

Results: The prevalence of diabetes and pre-diabetes was 14.0% (95% confidence interval [CI]: 13.2% to 14.8%) and 17.8% (95% CI: 17.0% to 18.7%) in the Southern Cone of Latin America, 9.8% (95% CI: 8.8% to 10.9%) and 17.1% (95% CI: 15.9% to 18.5%) in Peru, 19.0% (95% CI: 18.4% to 19.8%) and 24.0% (95% CI: 23.2% to 24.7%) in South Asia, and 13.8% (95% CI: 11.9% to 16.0%) and 9.9% (95% CI: 8.3% to 11.8%) in South Africa. The age- and sex-specific prevalence of diabetes and pre-diabetes for all countries increased with age ($p < 0.001$). In the Southern Cone of Latin America, Peru, and South Africa the prevalence of pre-diabetes rose sharply at 35 to 44 years. In South Asia, the sharpest rise in pre-diabetes prevalence occurred younger at 25 to 34 years. The prevalence of diabetes rose sharply at 45 to 54 years in the Southern Cone of Latin America, Peru, and South Africa, and at 35 to 44 years in South Asia. Diabetes and pre-diabetes prevalence increased with body mass index. South Asians had the highest prevalence of diabetes and pre-diabetes for any body mass index and normal-weight South Asians had a higher prevalence of diabetes and pre-diabetes than overweight and obese individuals from other regions. Across all regions, only 79.8% of persons with diabetes were aware of their diagnosis, of these only 78.2% were receiving treatment, and only 36.6% were able to attain glycemic control.

Conclusions: The prevalence of diabetes and pre-diabetes is alarmingly high among urban and periurban populations in Latin America, South Asia, and South Africa. Even more alarming is the propensity for South Asians to develop diabetes and pre-diabetes at a younger age and lower body mass index compared with individuals from other low and middle income countries. It is concerning that one-fifth of all people with diabetes were unaware of their diagnosis and that only two-thirds of those under treatment were able to attain glycemic control. Health systems and policy makers must make concerted efforts to improve diabetes prevention, detection, and control to prevent long-term consequences.

Diabetes mellitus is one of the leading causes of death and disability worldwide [1]. Globally, the number of people with diabetes is increasing because of population growth, aging, urbanization, increasing physical inactivity, and obesity. In 2014, the International Diabetes Federation estimated there were 387 million people with diabetes worldwide. This number is expected to rise to 592 million by 2035 [2]. Approximately 77% of people with diabetes live in low- and middle-income countries (LMICs) and these countries are projected to suffer the greatest increase in diabetes prevalence [2].

Accurate quantification of the prevalence, awareness, treatment, and control of diabetes is crucial for the planning and allocation of community and health resources in LMICs. Biochemical data from many LMICs have been lacking, and estimates of diabetes prevalence have been based largely on self-report, which may dramatically

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underestimate the true prevalence in countries with poor screening protocols and access to care [3]. Furthermore, prolonged untreated hyperglycemia can lead to significant microvascular and macrovascular damage resulting in neuropathy, nephropathy, retinopathy, and atherosclerosis [4-6]. Objectively collected data on diabetes treatment and control are therefore also needed to better inform health policy and medical intervention. Lastly, there is a paucity of data on the prevalence of pre-diabetes, which significantly increases the risk of future diabetes development [7]. Although the risk factors associated with diabetes and pre-diabetes are largely similar across populations, their expression and intensity may vary widely among ethnic groups and countries. Elucidation of different weight-related measures and how they relate to each other across different ethnicities contributes to the discourse regarding appropriate indicators for glucose monitoring and control.

Latin America, South Asia, and South Africa represent regions of the world undergoing rapid economic growth and social and demographic change. In addition, there is evidence that Latin Americans, South Asians, and those of African descent are more susceptible to developing diabetes [8-10]. We present data from population-based representative urban and periurban centers in the Southern Cone of Latin America (Argentina, Chile, and Uruguay), Peru, South Asia (India and Pakistan), and South Africa to quantify the prevalence of diabetes and pre-diabetes, proportions treated, and considered "controlled," and their relationship to metabolic risk factors by region.

RESEARCH DESIGN AND METHODS

The CESCAS I study is an observational prospective cohort study of 7,524 men and women, aged 35 to 74 years, recruited between February 2010 and December 2011 [11]. A 4-stage stratified sampling method was used to select a representative sample of the general population of the Southern Cone of Latin America. Participants were recruited from 4 mid-sized urban centers: Bariloche and Marcos Paz in Argentina, Temuco in Chile, and Pando-Barros Blancos in Uruguay. The overall response rate was 84.5% and was similar in men and women across different locations [11].

The CRONICAS study is a longitudinal cohort study of 3,601 men and women aged ≥35 years completed in 2010. Participants were randomly selected from 4 different geographic regions in Peru: Pampas de San Juan de Miraflores in Lima, Peru's capital and highly urban; Tumbes, a sea-level, semiurban area; and rural and urban sites in Puno, a high-altitude region 3,825 meters above sea level. Participants were identified using sex- and age-stratified sampling methods (35 to 44, 45 to 54, 55 to 64, ≥65 years). The overall response rate was 62.9% [12].

The CARRS study is a longitudinal cohort study of 14,317 men and women, aged ≥20 years, recruited from 2010 to 2011. Participants were recruited from 3 urban megacities: Chennai and New Delhi in India, and Karachi in Pakistan. Households were selected for participation using a multistage random sampling technique to achieve city-level representativeness. The overall response rate was 94.3%: Chennai, 90.9% (4,936); New Delhi, 98.9% (5,365); and Karachi, 94.3% (4,016) [13].

Finally, the CRIBSA study is a cross-sectional cohort study of 1,099 men and women, aged 25 to 74 years, from predominately black residential areas of Langa, Guguletu, Crossroads, Nyanga, and Khayelitsha in Cape Town. Between 2008 and 2009, participants were recruited using a 3-stage cluster sampling technique with pre-specified age and gender quotas to ensure at least 50 men and women were included in each gender category. The response rate was 84% in men and 87% in women [14].

We aggregated data among sites to obtain a total of 26,541 participants for analysis (Southern Cone of Latin America = 7,524; Peru = 3,601; South Asia = 14,317; South Africa = 1,099). From these 23,496 (88.5%) participants had data available for fasting blood glucose (Southern Cone of Latin America = 7,355 [97.8%], Peru = 3,135 [87.1%], South Asia = 11,907 [83.2%], South Africa = 1,099 [98.5%]).

Measurements

At all sites, comprehensive and uniform data collection instruments were used to capture measurements. A summary of all surveillance indicators, measures, methods, and instruments used in individual studies have been published in detail elsewhere [12,14-16]. Briefly, trained fieldworkers administered questionnaires to collect demographic, socioeconomic, and behavioral information and past and present health status of participants.

Anthropometric measurements included height, weight, and waist measurements using standardized techniques. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist circumference was taken at the midpoint between the lowest rib and top of the iliac crest. Three readings were taken and the mean of the 3 measurements was used. Blood pressure was recorded in the sitting position after 5 minutes of rest. In Argentina, a standardized mercury or aneroid sphygmomanometer with an adequate cuff size was used. The cuff was placed on the right arm of the participant and inflated until it reached a pressure of 30 mm Hg above the level at which the radial pulse can no longer be palpated. Three measurements were obtained with 30-second intervals between them. The average of the 3 values was used. In India, Peru, and South Africa, systolic and diastolic blood pressure were measured in triplicate using an automatic monitor OMRON HEM-780 previously validated for the adult population [17]. The average of 3 measurements was used.

Fasting blood samples were collected by venipuncture at field sites and transported in cold chain to central laboratories in their respective countries. Sample aliquots were stored in cyro-vials at −70°C to −80°C for future studies.

Self-reported diabetes was defined as subjects with self-reported history of diabetes and/or on drug treatment for diabetes. Diabetes was defined as either a prior diagnosis of diabetes on treatment or fasting plasma glucose (FPG) ≥126 mg/dl. Pre-diabetes was defined as no prior diagnosis of diabetes and FPG 100 to 125 mg/dl [18]. Dysglycemia was defined as the presence of either pre-diabetes or diabetes. Treatment for diabetes was defined as self-reported use of oral hypoglycemic medications or insulin. Control of diabetes was defined as those under treatment for diabetes with FPG <130 mg/dl.

Hypertension was defined as a mean systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, and/or self-report of current use of antihypertensive medications [19]. Hypercholesterolemia was defined as total cholesterol ≥200 mg/dl or 11.1 mmol/l, hypertriglyceridemia was defined as triglycerides ≥150 mg/dl or 1.7 mmol/l, and low high-density lipoprotein cholesterol (HDL-C) was defined as <40 mg/dl or 1.0 mmol/l (males) and <50 mg/dl or 1.3 mmol/l (females). Overweight and obesity was defined as BMI ≥25 kg/m^2 and abdominal obesity was defined as waist circumference ≥90 cm (males) and ≥80 cm (females) using population-specific guidelines [20]. A waist-to-height ratio cutoff of ≥0.5 was used because it has been shown to be a risk factor for the development of cardiovascular disease and diabetes [21].

Statistical analysis

Prevalence with 95% confidence intervals (CI) for diabetes and pre-diabetes were estimated for each country. Estimates of continuous variables were summarized as mean (95% CI) for normally distributed data or proportions (95% CI) for categorical variables. Comparison of means of quantitative variables across different diabetes categories was done by analysis of variance for normal data. Association between categorical variables was checked using chi-square testing.

Bivariate regression analysis was performed first and then multinomial logistic regression analysis was performed to assess the association between risk factors with diabetes and pre-diabetes using normoglycemia as the reference category. The odds ratio of diabetes and pre-diabetes and their 95% CI were estimated for all countries together after controlling for country, gender, age per 10-year increment, current use of smoking, generalized obesity, abdominal obesity, waist to height ratio, hypertension, hypercholesterolemia, hypertriglyceridemia, and low HDL-C. Statistical analyses were done using STATA version 12.1 (StataCorp LP, College Station, TX).

RESULTS

The age-standardized and weighted prevalence of diabetes, pre-diabetes, and dysglycemia for the 4 regions are shown in Table 1. The prevalence of diabetes was 14.0% (95% CI: 13.2% to 14.8%) in the Southern Cone of Latin America, 9.8% (95% CI: 8.8% to 10.9%) in Peru, 19.0% (95% CI: 18.4% to 19.8) in South Asia, and 13.8% (95% CI: 11.9% to 16.0%) in South Africa. The prevalence of pre-diabetes was 17.8% (95% CI: 17.0% to 18.7%) in the Southern Cone of Latin America, 17.1% (95% CI: 15.9% to 18.5%) in Peru, 24.0% (95% CI: 23.2% to 24.7%) in South Asia, and 9.9% (95% CI: 8.3% to 11.8%) in South Africa. The prevalence of any dysglycemia was 31.8% (95% CI: 30.7% to 32.9%) in the Southern Cone of Latin America, 27.0% (95% CI: 25.4% to 28.5%) in Peru, 43.0% (95% CI: 42.1% to 43.0%) in South Asia, and 23.7% (95% CI: 21.3% to 26.4%) in South Africa. Overall, men had a higher prevalence of pre-diabetes and dysglycemia compared with women, whereas women had a higher prevalence of diabetes.

The age- and sex-specific prevalence of diabetes and pre-diabetes for all countries is shown in Figure 1. In all countries, the prevalence of both diabetes and pre-diabetes increased with age ($p < 0.001$ for trend). In the Southern Cone of Latin America, Peru, and South Africa the prevalence of pre-diabetes rose sharply at 35 to 44 years. In South Asia, the sharpest rise in pre-diabetes prevalence occurred younger at 25 to 34 years. In alignment with this, the prevalence of diabetes rose sharply at 45 to 54 years in the Southern Cone of Latin America, Peru, and South Africa; and at 35 to 44 years in South Asia. In the Southern Cone of Latin America, Peru, and South Africa there was a gradual increase in diabetes prevalence with age with the highest prevalence among those older than 65 years. However, in South Asia the prevalence of diabetes declined after 65 years in men. In the Southern Cone of Latin America, men had a higher prevalence of pre-diabetes at

TABLE 1. Prevalence of pre-diabetes, diabetes, and dysglycemia

	Southern Cone of Latin America (n = 7,355)	South Asia (n = 11,907)	Peru (n = 3,119)	South Africa (n = 1,099)	Total (n = 23,480)
Diagnosis	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Pre-Diabetes	17.8 (17.0–18.7)	24.0 (23.2–24.7)	17.1 (15.9–18.5)	9.9 (8.3–11.8)	20.5 (20.0–21.0)
Diabetes	14.0 (13.2–14.8)	19.0 (18.4–19.8)	9.8 (8.8–10.9)	13.8 (11.9–16.0)	16.0 (15.5–16.5)
Dysglycemia	31.8 (30.7–32.9)	43.0 (42.1–43.9)	27.0 (25.4–28.5)	23.7 (21.3–26.4)	36.5 (35.8–37.1)

CI, confidence interval.

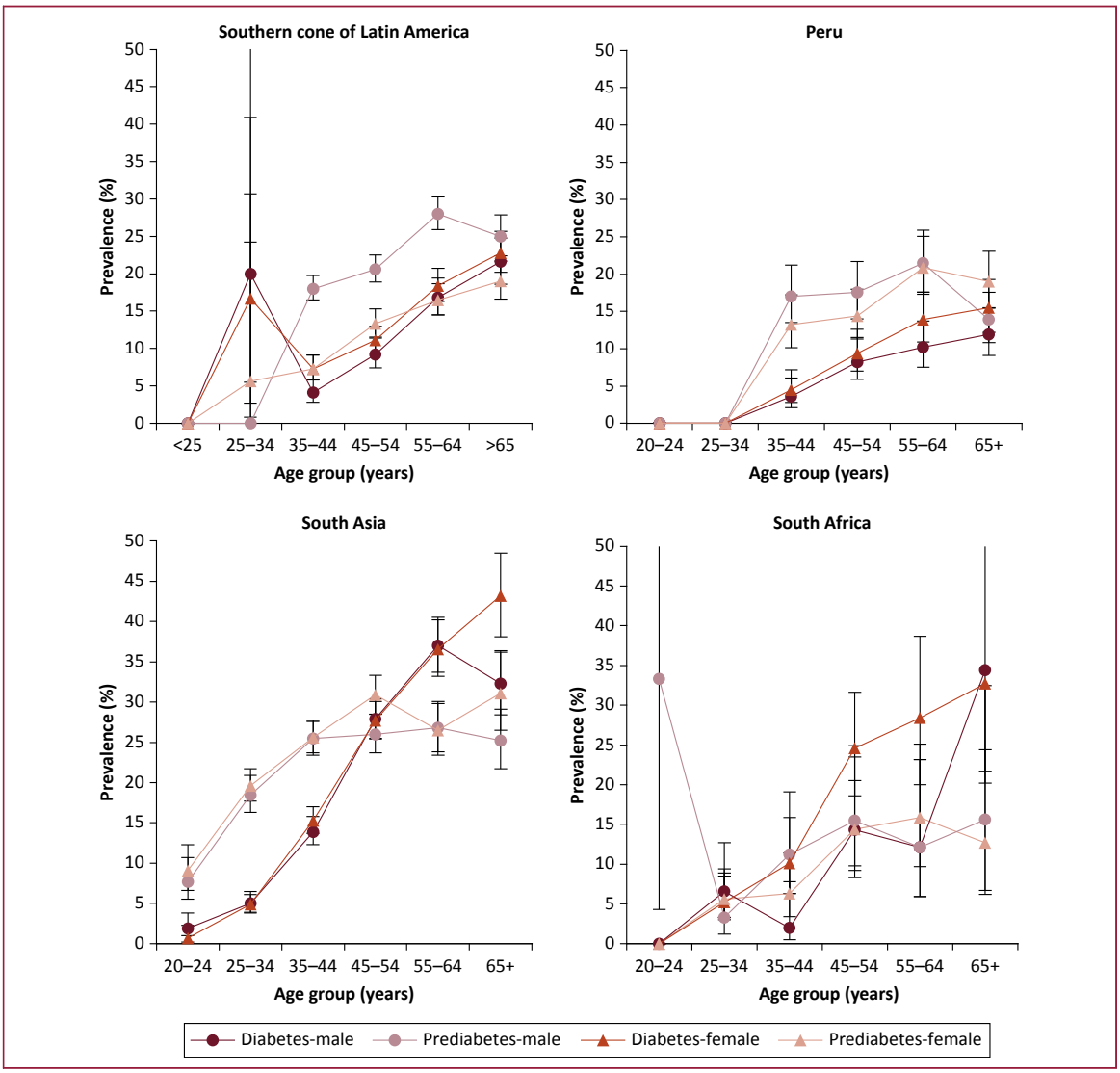

FIGURE 1. Age- and sex-specific prevalence of diabetes and pre-diabetes.

every age group compared with women. However, this did not correspond with an overall difference in diabetes prevalence between men and women (Figure 1).

Participant characteristics based on glycemic status are summarized in Table 2. All countries followed similar trends: participants with normal fasting glucose were younger and had a lower BMI, waist circumference, triglycerides, low-density lipoprotein cholesterol, systolic and diastolic blood pressure, and higher HDL-C than those with pre-diabetes and diabetes. South Asia was home to the youngest population of adults with diabetes, with the lowest BMI and waist circumference. Participants from South Africa had significantly lower levels of total cholesterol compared with the total population median for those with no diabetes, those with pre-diabetes, and those with diabetics, respectively.

The prevalence of diabetes and pre-diabetes increased with increasing BMI categories (normal weight, overweight, and obese) (Figure 2). Among normal-weight individuals there was no significant difference in diabetes or pre-diabetes prevalence in Peru, South Africa, or the Southern Cone of Latin America. South Asians had the highest prevalence of diabetes and pre-diabetes for every BMI category. Normal-weight South Asians had a higher prevalence of diabetes and pre-diabetes than overweight individuals from Peru, South Africa, or the Southern Cone of Latin America. Peru had the lowest prevalence of diabetes in overweight and obese individuals. South Africa had the lowest prevalence of pre-diabetes among all BMI categories (Figure 2).

Results from standardized multinomial logistic regression models created with normoglycemia as a

TABLE 2. Subject characteristics by diabetes status

	No DM	PDM	DM
Southern Cone of Latin America	n = 5,016	n = 1,310	n = 1,029
Age, yrs	52.7 (52.4–53.0)	56.6 (56.0–57.1)	59.0 (58.4–59.6)
Male, %	63.9 (62.2–65.6)	23.1 (21.7–24.6)	13.0 (11.9–14.2)
BMI, kg/m^2	28.2 (28.0–28.3)	30.5 (30.2–30.8)	32.1 (31.7–32.5)
WCC, cm	94.2 (93.8–94.6)	101.2 (100.5–101.9)	104.8 (103.9–105.6)
SBP, mm Hg	127.2 (126.7–127.8)	135.8 (134.7–137.0)	138.0 (136.7–139.3)
DBP, mm Hg	81.6 (81.3–81.9)	85.2 (84.5–85.8)	83.3 (82.6–84.0)
Total cholesterol, mg/dl	203.8 (202.6–205.0)	206.2 (203.9–208.4)	200.8 (197.8–203.7)
Triglycerides, mg/dl	141.6 (138.5–144.6)	174.1 (167.4–180.9)	195.3 (185.3–205.4)
HDL-C, mg/dl	47.5 (47.2–47.9)	44.9 (44.2–45.6)	44.1 (43.4–44.8)
LDL-C, mg/dl	n/a	n/a	n/a
India	n = 6,787	n = 2,852	n = 2,268
Age, yrs	39.1 (38.8–39.4)	45.2 (44.7–45.7)	51.2 (50.7–51.6)
Male, %	57.4 (56.1–58.7)	23.1 (22.1–24.3)	19.5 (18.5–20.5)
BMI, kg/m^2	24.4 (24.2–24.5)	26.5 (26.3–26.7)	27.2 (27.0–27.5)
WCC, cm	83.3 (83.0–83.6)	89.4 (88.9–89.9)	92.7 (92.2–93.3)
SBP, mm Hg	119.4 (119.0–119.9)	127.2 (126.4–127.9)	133.3 (132.4–134.3)
DBP, mm Hg	79.9 (79.6–80.2)	84.3 (83.8–84.7)	85.7 (85.2–86.2)
Total cholesterol, mg/dl	174.3 (173.4–175.2)	184.1 (182.7–185.6)	188.8 (187.1–190.5)
Triglycerides, mg/dl	130.2 (127.8–132.5)	152.5 (149.1–155.8)	188.3 (183.0–193.6)
HDL-C, mg/dl	44.0 (43.7–44.3)	43.7 (43.3–44.1)	41.8 (41.4–42.3)
LDL-C, mg/dl	106.7 (106.0–107.5)	111.9 (110.7–113.1)	113.1 (111.7–114.5)
Peru	n = 2,290	n = 537	n = 308
Age, yrs	54.9 (54.4–55.5)	56.1 (55.1–57.1)	59.8 (58.6–61.0)
Male, %	74.0 (71.7–76.1)	17.4 (15.6–19.4)	8.6 (7.3–10.1)
BMI, kg/m^2	26.9 (26.8–27.1)	29.3 (28.9–29.7)	29.8 (29.2–30.3)
WCC, cm	90.2 (89.8–90.7)	95.6 (94.7–96.5)	97.9 (96.7–99.0)
SBP, mm Hg	116.9 (116.2–117.7)	123.8 (122.1–125.5)	126.4 (124.0–128.8)
DBP, mm Hg	72.6 (72.2–73.0)	76.0 (75.1–76.9)	77.0 (75.5–78.5)
Total cholesterol, mg/dl	197.0 (195.4–198.6)	207.0 (203.6–210.4)	208.4 (203.3–213.6)
Triglycerides, mg/dl	147.5 (144.2–150.8)	188.8 (177.7–199.9)	203.6 (187.1–220.1)
HDL-C, mg/dl	42.3 (41.9–42.8)	39.0 (38.1–39.9)	40.3 (39.0–41.6)
LDL-C, mg/dl	107.0 (94.4–119.6)	80.6 (64.3–96.9)	103.0 (76.1–129.9)
South Africa	n = 838	n = 109	n = 152
Age, yrs	41.3 (40.4–42.1)	48.3 (46.0–50.6)	52.1 (50.2–54.1)
Male, %	79.5 (75.3–83.2)	10.4 (7.7–13.8)	10.1 (7.5–13.5)
BMI, kg/m^2	28.6 (28.1–29.2)	32.6 (30.8–34.5)	33.6 (32.4–34.9)
WCC, cm	90.4 (89.4–91.4)	98.1 (95.0–101.2)	102.4 (100.1–104.7)
SBP, mm Hg	123.4 (121.9–124.9)	133.5 (129.4–137.5)	137.4 (133.1–141.6)
DBP, mm Hg	80.7 (79.8–81.6)	86.6 (84.0–89.1)	86 (83.9–88.1)
Total cholesterol, mg/dl	77.6 (76.3–78.9)	84.6 (80.6–88.6)	86.8 (83.0–90.6)
Triglycerides, mg/dl	18.6 (17.6–19.6)	24 (21.4–26.5)	29 (25.2–32.7)
HDL-C, mg/dl	21.1 (20.5–21.7)	22.7 (21.0–24.4)	20.3 (19.3–21.4)
LDL-C, mg/dl	52.8 (51.7–53.9)	57.1 (53.8–60.4)	61.4 (58.2–64.6)
Cholesterol/HDL-C	4 (3.9–4.0)	4 (3.8–4.3)	4.5 (4.3–4.7)
Triglyceride/HDL-C	1 (0.9–1.1)	1.2 (1.1–1.4)	1.6 (1.3–1.9)
Total	n = 14,931	n = 4,808	n = 3,757
Age, yrs	46.2 (46.0–46.4)	49.6 (49.2–49.9)	54.1 (53.7–54.4)
Male, %	62.5 (61.5–63.4)	21.8 (21.1–22.6)	15.7 (15.0–16.4)
BMI, kg/m^2	26.5 (26.4–26.6)	28.2 (28.0–28.4)	29.3 (29.0–29.5)
WCC, cm	88.5 (88.3–88.8)	93.6 (93.2–94.0)	97.0 (96.5–97.4)

(continued)

TABLE 2–*continued*. Subject characteristics by diabetes status

	No DM	PDM	DM
SBP, mm Hg	121.9 (121.6—122.3)	129.3 (128.8—129.9)	134.2 (133.5—135.0)
DBP, mm Hg	79.4 (79.2—79.6)	83.6 (83.3—84.0)	84.3 (83.9—84.7)
Total cholesterol, mg/dl	182.3 (181.6—183.1)	190.5 (189.2—191.7)	189.6 (188.0—191.2)
Triglycerides, mg/dl	130.5 (128.9—132.1)	159.6 (156.5—162.6)	185.1 (180.5—189.7)
HDL-C, mg/dl	43.7 (43.5—43.9)	43.1 (42.7—43.4)	41.4 (41.1—41.8)
LDL-C, mg/dl	100.9 (100.1—101.6)	109.6 (108.3—110.8)	109.7 (108.2—111.1)

Values are median (interquartile range).

BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; n/a, not available; PDM, pre-diabetes mellitus; SBP, systolic blood pressure; WCC, waist circumference.

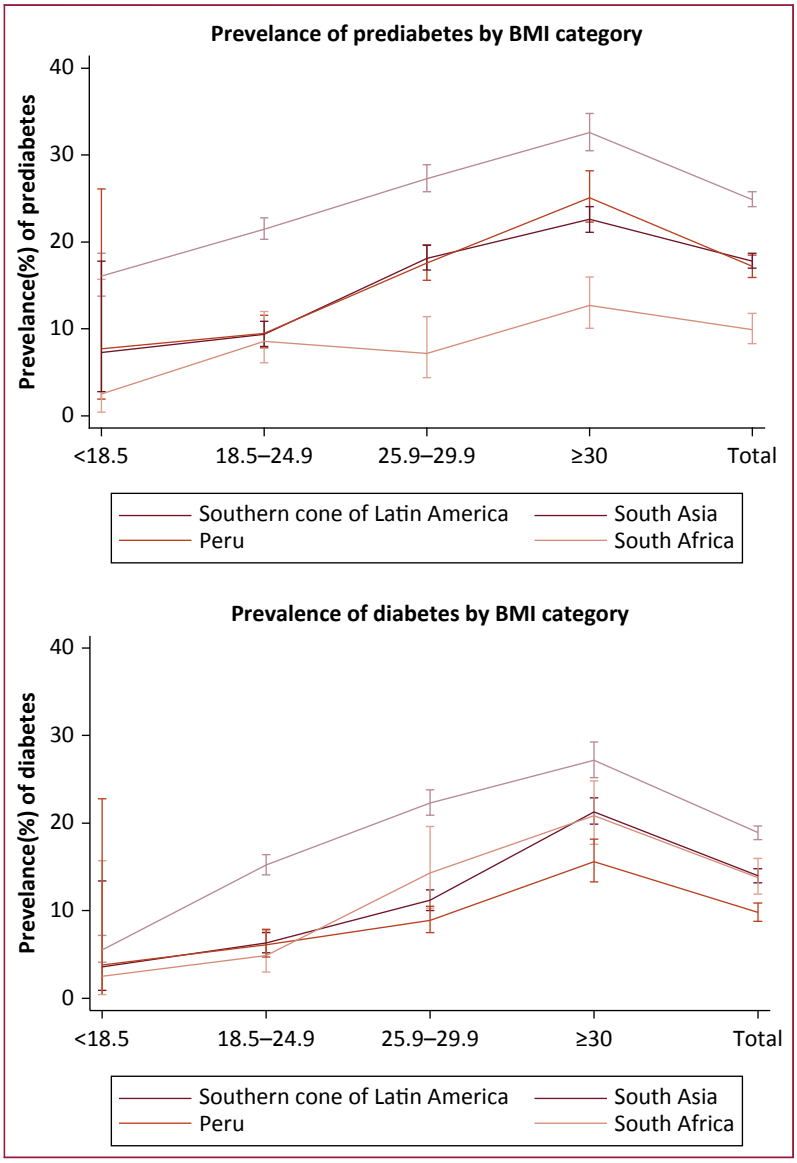

FIGURE 2. Prevalence of diabetes and pre-diabetes by body mass index category. BMI, body mass index.

reference group are summarized in Tables 3 and 4. Overall, older age, overweight and obesity, abdominal obesity, hypertension, hypertriglyceridemia, and increased waist-to-height ratio were significantly associated with higher odds of having either diabetes or pre-diabetes. Male gender was associated with decreased odds of having pre-diabetes, whereas having a low HDL-C increased the odds of having diabetes. Using South Africa as the reference group, South Asians were 3.55 times more likely (95% CI: 2.85 to 4.41) to have pre-diabetes and 2.09 times more likely (95% CI: 1.70 to 2.57) to have diabetes. In contrast, Southern Latin Americans were half as likely to have diabetes (0.48 [95% CI: 0.39 to 0.60]) and Peruvians were one-third as likely to have diabetes (0.35 [95% CI: 0.27 to 0.44]) than South Africans.

Participants in South Asia and the Southern Cone of Latin America had the greatest awareness of diabetes status (81.7% and 81.2%, respectively), whereas South Africa had the lowest (65.5%) (Figure 3). Across all 4 sites only 20.2% of persons with diabetes were unaware of their diagnosis. Peru had the highest percentage of persons with diabetes aware of their disease on treatment (90.9%), whereas South Africa had the lowest (59.0%) (Figure 3). Peru and the Southern Cone of Latin America had the highest percentage of treated persons with diabetes who attained glycemic control (48.5% and 48.3%, respectively), whereas South Asia had the lowest (29.6%). Across all 4 sites, only 36.6% of persons with diabetes receiving treatment were able to attain glycemic control (Figure 3).

DISCUSSION

In this study of 4 regions with representative, recent data from large urban and periurban centers in the Southern Cone of Latin America, South Asia, Peru, and South Africa, we found that 1 in 5 adults had pre-diabetes, 1 in 6 had diabetes, 1 in 5 were unaware of their diagnosis, and 1 in 3 had dysglycemia. South Africa had the lowest prevalence of diabetes and pre-diabetes, whereas South Asia had the highest. South Asians were more likely to have dysglycemia at a younger age, lower BMI, and waist circumference. South Asia had the highest percentage of persons with

TABLE 3. Risk factors associated with diabetes

Risk Factors	Southern Cone of Latin America	South Asia	Peru	South Africa	Total
Age (per 10-year increment)	1.04 (1.04–1.05)	1.06 (1.05–1.06)	1.03 (1.02–1.04)	1.04 (1.02–1.06)	1.05 (1.05–1.05)
Male	1.03 (0.89–1.20)	1.01 (0.88–1.15)	1.07 (0.82–1.39)	0.76 (0.46–1.26)	0.98 (0.89–1.07)
Current smoking	0.80 (0.67–0.96)	0.91 (0.78–1.06)	n/a*	0.83 (0.47–1.46)	0.88 (0.79–0.99)
Obesity (BMI ≥25 kg/m^2)	1.67 (1.29–2.17)	1.31 (1.13–1.53)	1.18 (0.80–1.75)	2.03 (0.91–4.51)	1.39 (1.24–1.57)
Abdominal obesity†	1.75 (1.19–2.60)	1.41 (1.16–1.70)	2.78 (1.63–4.72)	2.38 (0.79–7.18)	1.61 (1.38–1.88)
Waist to height ratio‡	1.33 (0.81–2.19)	1.79 (1.43–2.24)	0.96 (0.44–2.09)	1.17 (0.37–3.63)	1.63 (1.34–1.97)
Hypertension§	1.91 (1.62–2.24)	2.13 (1.88–2.42)	2.85 (2.19–3.70)	3.35 (2.08–5.39)	1.48 (1.41–1.55)
Hypercholesterolemia‖	0.68 (0.59–0.80)	1.12 (0.98–1.28)	1.05 (0.80–1.37)	n/a	0.93 (0.85–1.02)
Hypertriglyceridemia¶	2.04 (1.75–2.38)	2.31 (2.02–2.64)	2.17 (1.64–2.88)	17.13 (1.16–252.62)	2.21 (2.01–2.43)
Low HDL-C#	1.34 (1.15–1.57)	1.13 (0.99–1.29)	1.04 (0.76–1.41)	n/a	1.22 (1.11–1.35)

The table displays the associations (adjusted odds ratios [95% confidence intervals]) between each risk factor and diabetes adjusted for all other risk factors in the table. The "Total" column displays associations pooled across all 4 countries and are additionally adjusted for country. Abbreviations as in Table 2.

*No concomitant current smokers and persons with diabetes.

†Waist ≥90 cm for male and ≥80 cm for female.

‡Waist to height ratio ≥0.5.

§Self-reported hypertension and/or blood pressure ≥140/90 mm Hg.

‖Hypercholesterolemia ≥200 mg/dl.

¶Hypertriglyceridemia ≥150 mg/dl.

#Low HDL-C <40 mg/dl for males and <50 mg/dl for females.

diabetes aware of their diagnosis, whereas South Africa had the lowest. Peru had the highest percentage of persons with diabetes under treatment and South Africa had the lowest. Overall, less than four-fifths of all persons with diabetes aware of their diagnosis in the Southern Cone of Latin America, Peru, South Asia, and South Africa were receiving treatment for diabetes. Countries in the Southern Cone of Latin America and Peru had the highest percentage of controlled diabetes, whereas South Asia had the lowest. Across all countries, approximately two-thirds of all persons with diabetes on treatment had control of their disease.

TABLE 4. Risk factors associated with pre-diabetes

Risk Factors	Southern Cone of Latin America	South Asia	Peru	South Africa	Total
Age (per 10-year increment)	1.03 (1.02–1.03)	1.03 (1.02–1.03)	1.01 (1.00–1.02)	1.02 (1.00–1.04)	1.02 (1.02–1.03)
Male	0.55 (0.48–0.62)	1.02 (0.91–1.14)	0.82 (0.67–1.01)	0.62 (0.36–1.06)	0.77 (0.72–0.84)
Current smoking	0.86 (0.74–1.00)	0.87 (0.76–1.00)	n/a*	0.89 (0.50–1.56)	0.83 (0.76–0.92)
Obesity (BMI ≥25 kg/m^2)	1.69 (1.35–2.11)	1.39 (1.22–1.59)	1.63 (1.18–2.26)	1.06 (0.50–2.25)	1.53 (1.38–1.70)
Abdominal obesity†	1.74 (1.28–2.36)	1.16 (0.99–1.36)	1.97 (1.35–2.86)	1.90 (0.70–5.17)	1.40 (1.23–1.59)
Waist to height ratio‡	1.05 (0.72–1.53)	1.37 (1.16–1.62)	0.80 (0.47–1.35)	1.00 (0.39–2.60)	1.16 (1.01–1.34)
Hypertension§	1.42 (1.24–1.64)	1.33 (1.19–1.48)	1.50 (1.20–1.86)	2.52 (1.55–4.08)	1.19 (1.14–1.24)
Hypercholesterolemia‖	0.89 (0.78–1.02)	1.03 (0.91–1.16)	1.19 (0.97–1.47)	n/a	0.99 (0.91–1.07)
Hypertriglyceridemia¶	1.54 (1.34–1.77)	1.48 (1.32–1.67)	1.49 (1.20–1.85)	0.00 (0.00–0.00)	1.52 (1.40–1.64)
Low HDL-C#	1.15 (1.00–1.32)	0.88 (0.79–0.98)	1.23 (0.97–1.56)	n/a	1.03 (0.95–1.12)

The table displays the associations (adjusted odds ratios [95% confidence intervals]) between each risk factor and pre-diabetes adjusted for all other risk factors in the table. The "Total" column displays associations pooled across all 4 countries and are additionally adjusted for country. OR, odds ratio; other abbreviations as in Tables 1 and 2.

*No concomitant current smokers and persons with pre-diabetes.

†Waist ≥90 cm for male and ≥80 cm for female.

‡Waist to height ratio ≥0.5.

§Self-reported hypertension and/or blood pressure ≥140/90 mm Hg.

‖Hypercholesterolemia ≥200 mg/dl.

¶Hypertriglyceridemia ≥150 mg/dl.

#Low HDL-C <40 mg/dl for males and <50 mg/dl for females.

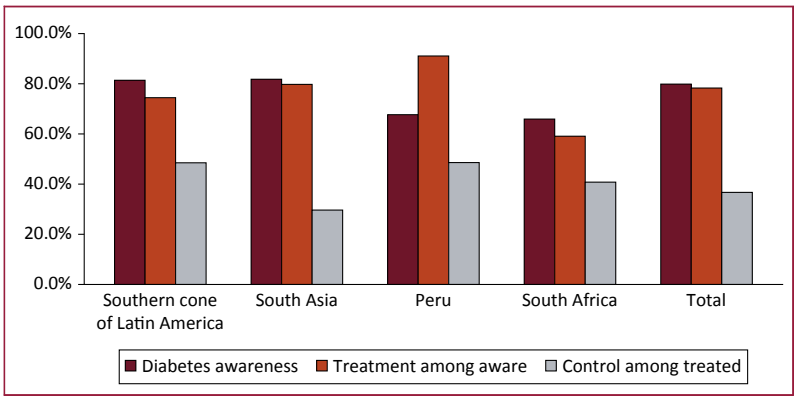

FIGURE 3. Diabetes awareness, treatment, and control.

There are multiple epidemiological studies available on the prevalence of pre-diabetes and diabetes in the Southern Cone of Latin America, South Asia, Peru, and South Africa [22-26]. However, they are not directly comparable with our study because of the following reasons: 1) many have relied on self-report to calculate diabetes prevalence [22]; 2) they combined participants from urban and rural areas and results for large metropolitan cities were not presented separately [25]; 3) they used different methodology and sampling techniques [23]; or 4) diabetes and pre-diabetes were diagnosed using alternative testing methods, such as the 75-g oral glucose tolerance test, which can dramatically affect population estimates of diabetes prevalence [26,27].

In the current study, the prevalence of pre-diabetes rose sharply at 35 to 44 years in the Southern Cone of Latin America, Peru, and South Africa, but much earlier in South Asia at 25 to 34 years of age. As expected, the prevalence of diabetes rose sharply at 45 to 54 years of age in the Southern Cone of Latin America, Peru, and South Africa, but was much earlier in South Asia at 35 to 44 years of age. The higher prevalence of diabetes among young South Asians relative to other groups is a matter of concern because the microvascular and macrovascular complications of diabetes are directly related to prolonged exposure to hyperglycemia [4-6]. The earlier onset of pre-diabetes and diabetes in South Asians may be attributed to both genetic (increased genetic susceptibility and propensity for abdominal fat accumulation) [28-30] and environmental (sedentary lifestyle, increased consumption of white rice and use of refined grains, and use of trans and saturated fats in cooking) [31] causes. In addition, poor nutrition in utero has been shown to result in permanent changes in insulin-glucose metabolism, resulting in decreased glucose tolerance in adulthood [32,33]. This highlights the importance of interventions directed at young South Asians to encourage healthier food preparation practices and increase physical activity. In addition, improving the nutrition of pregnant women may be a cost-effective means to reduce the development of glucose later in life [32].

In all countries there was an age-associated increase in diabetes prevalence with the highest being among those older than 65 years of age. However, in South Asia, we found the prevalence of diabetes declined after 65 years in men, which may reflect greater diabetes-related mortality in this subgroup. Peru had the lowest prevalence among those >65 years of age (11.9% in men and 15.5% in women), whereas South Africa had the highest (34.4% in men and 32.7% in women). This is a cause for concern because many LMICs have a growing proportion of individuals older than 65 years, as a result of increasing life expectancies and declining birth rates. For example, in South Africa the average life expectancy has steadily increased from 52 years in 2005, to 61 years in 2014 [34]. Improved access to highly active retroviral therapy for the treatment of human immunodeficiency virus/AIDS has also contributed to increased life expectancy in this region [35]. However, use of protease inhibitors and nucleoside reverse transcriptase inhibitors has been shown to result in insulin resistance and dyslipidemia [36]. As a result, noncommunicable diseases are emerging in rural and urban areas, most prominently among poor people living in urban settings [37]. This growth of a chronically ill, ageing population increases the short- and long-term pressure on health care services.

In the current study, only a 65% to 82% of all persons with diabetes were aware of their diagnosis; of these, only 59% to 91% of was receiving treatment. The highest percentage of persons with diabetes receiving treatment was in Peru (90.9%) and the lowest was in South Africa (59.0%). Only one-quarter to one-half of all persons with diabetes were able to attain control of their disease. Peru had the highest percentage of treated persons with diabetes who were able to attain good glycemic control (48.5%), whereas South Asia had the lowest (29.6%). This is alarming because complications from diabetes are directly related to exposure to hyperglycemia. High blood glucose levels accounted for 21% of all deaths from ischemic heart disease and 13% of all deaths from stroke worldwide with 84% of these cardiovascular deaths occurring in LMICs [38]. Diabetes is the most common underlying cause of chronic kidney disease, and diabetic retinopathy is the leading cause of blindness in working-age adults in many countries [39,40]. Improvement in glycemic control is the key for preventing diabetes-related complications [41]. Our study indicates that awareness, treatment, and control rates of diabetes in the urban and periurban populations in Chile, Uruguay, Argentina, India, Pakistan, Peru, and South Africa are disproportionally low, which raises concern for high rates of diabetes-related complications and mortality over time.

Strengths and limitations

One of the limitations of this study is its cross-sectional nature, which prevents determination of the causal pathways underlying reported relationships between diabetes and its risk factors. Another limitation is that extrapolation of the study results to the entire country is difficult, because data came from predominately urban and

periurban areas with rural areas being underrepresented. Finally, only FPG was used instead of an oral glucose tolerance test, which is considered the gold standard method for diagnosis of diabetes. The strengths of the study are that it is population-based; large; and representative of the general population of 4 urban and periurban areas from the Southern Cone of Latin America, Peru, South Asia, and South Africa. In addition, data were collected homogeneously from their respective sites, which allows for direct comparisons to be made among countries.

CONCLUSIONS

Diabetes and pre-diabetes prevalence are alarmingly high among urban and periurban populations in Latin America, South Asia, and South Africa. Even more alarming is the increased prevalence of dysglycemia in South Asians at younger ages and lower BMIs compared with individuals from other countries. It is a matter of concern that 20% of persons with diabetes were unaware of their diagnosis, and that only 80% of those aware were receiving treatment for their disease, with only 40% being able to attain good glycemic control. Among all regions, South Asia was home to the most persons with diabetes and had the lowest rates of glycemic control. Concerted measures to raise public awareness of diabetes and the development of effective methods to appropriately screen for diabetes and pre-diabetes in this population are desperately needed. Furthermore, existing health care infrastructure must be expanded to improve the quality of diabetes care and control. Finally, the advertisement and adoption of healthy lifestyles, especially in urban areas and in South Asia where diabetes prevalence is the highest and affects a younger population, is urgently needed for primary prevention and to improve glycemic control in those whose have already developed diabetes to prevent long-term complications.

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