Elevated incidence rates of diabetes in Peru: report from PERUDIAB, a national urban population-based longitudinal study

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ABSTRACT

Objective A recent report from a non-nationally representative, geographically diverse sample in four separate communities in Peru suggests an unusually high diabetes incidence. We aimed to estimate the national diabetes incidence rate using PERUDIAB, a probabilistic, national urban population-based longitudinal study.

Research design and methods 662 subjects without diabetes, selected by multistage, cluster, random sampling of households, representing the 24 administrative and the 3 (coast, highlands and jungle) natural regions across the country, from both sexes, aged 25+ years at baseline, enrolled in 2010–2012, were followed for 3.8 years. New diabetes cases were defined as fasting blood glucose ≥126 mg/dL or on medical diabetes treatment.

Results There were 49 cases of diabetes in 2408 person-years follow-up. The weighted cumulative incidence of diabetes was 7.2% while the weighted incidence rate was estimated at 19.5 (95% CI 13.9 to 28.3) new cases per 1000 person-years. Older age, obesity and technical or higher education were statistically associated with the incidence of diabetes.

Conclusion Our results confirm that the incidence of diabetes in Peru is among the highest reported globally. The fast economic growth in the last 20 years, high overweight and obesity rates may have triggered this phenomenon.

INTRODUCTION

Diabetes mellitus is a global problem. The WHO has estimated that in 2014 there were 422 million adults with diabetes throughout the world, having quadrupled since 1980.[1] This increase appears to be primarily coupled with rising obesity rates which have increased significantly, especially in low/middle-income countries (LMIC).[2] The consequences for the health systems and countries would be shocking, and a recent meta-analysis has estimated the direct annual medical costs at $825 billion (US$),[3 4] a figure accumulated using the countries for which the information is available. All this information has been deduced from reports on the population

Significance of this study

What is already known about this subject?
► There are no nationally representative reports of incidence of diabetes in Peru. A population-based study in four dispersed communities suggests that the incidence could be high.

What are the new findings?
► After 4 years follow-up, the cumulative incidence and the incidence rate of diabetes were estimated at 7.2% and 19.5 new cases per 1000 person-years, respectively.
► Our results confirm that the incidence of diabetes in Peru is among the highest reported globally.

How might these results change the focus of research or clinical practice?
► Our results might hasten the academia and public interest, resulting in renewed efforts to design effective public health policies.

prevalence of diabetes, which are generally very frequent in the literature.[2 3 5]

In contrast, reports on the population incidence of diabetes, which allow estimating the growth rate of the disease, are much rarer, especially in LMIC. According to information available, global extremes of population incidence of type 2 diabetes appear to have been established between 33.1 per 1000 person-years for the Indo-Asian population in Chennai, India[6] and 0.6 per 1000 person-years in Denmark as for 2011.[7]

Recently, our group reported that by 2012, the prevalence of type 2 diabetes in Lima metro, Peru's capital city, had doubled to 8.2% in just 7 years.[8] Moreover, a recent single report from a population-based, non-nationally representative, geographically diverse sample in four separated communities in Peru suggests an unusually high diabetes incidence.[9] We aimed to estimate the national

diabetes incidence rate using PERUDIAB, a probabilistic, national urban population-based longitudinal study.

RESEARCH DESIGN AND METHODS

Baseline survey

PERUDIAB is a longitudinal and probabilistic population-based three-wave study based on households, designed to obtain national estimates of the most important features of type 2 diabetes and related diseases, and its design has been previously described in detail.[8] In short, the original design was a national probabilistic cluster sample, which included 24 administrative regions and the three natural regions of Peru, stratified according to population density, based on the cartographic material prepared by the National Institute of Statistics and Informatics of Peru (Instituto Nacional de Estadística e Informática), based on the population census of 2007. The clusters were selected randomly and independently for each administrative region and corresponded to approximately 120 households, which were randomly selected, and of these, a person with 25+ years by systematic sampling based on the date of their next birthday. All regions of the country were included. Rural areas were not included, which hold approximately 15% of the country's population.

The survey of the first wave (baseline) took place between 2010 and 2012, and enrolled 1677 residents in the urban and urban fringe area of Peru, 25 years or older, both sexes, who lived in the sampled household, including their in-house domestic and personal service. We defined household to include paid shelters hosting up to nine persons and any person who does not belong to the family but was hosted for the last consecutive 30 days. We excluded patients with mental disorders and pregnant women. A signed informed consent was required to participate in the study. The study protocol was approved by a nationally accredited ethics committee.

The questionnaires were tested through a pilot study, and to maximize response, households were visited by trained health personnel living in the sampled area. Data were independently validated face-to-face or by telephone by the staff who did not know the results of the initial survey.

Blood specimens were obtained early in the morning, after a verified fasting period of 12 hours, or if verification was in doubt, a new specimen was required at a later date. Venous blood was deposited in special tubes to stop the consumption of glucose,[10] the plasma was separated within 2 hours and sent under cold chain conditions to the central laboratory for processing using glucose oxidase spectrometric assays.

Follow-up survey

The procedures used during the fieldwork in the follow-up were essentially the same as in the first wave. Between July 2014 and February 2015 we were able to contact 713 subjects who participated in the first wave, which agreed to undergo interview, physical examination and complete blood analysis. The non-response (attrition) analysis (detailed in statistical methods) showed that the diagnosis of diabetes at baseline was not statistically associated with non-response. The resulting sample includes clusters of all 24 administrative regions of Peru and its three natural regions, appropriately reflecting the variability of the country.

Definitions

For the present study, the following definitions apply: Diabetes: fasting plasma glucose ≥126 mg/dL or receiving medical diabetes treatment (oral anti-diabetes drugs and/or insulin), which should have started during the follow-up period. For predictor variables, the baseline statuses according to the following definitions were used: level of education: <7 years (primary or lower), 7–11 (secondary), 12+ (technical or higher). Body mass index (BMI): <25 (normal), 25–29.9 (overweight), ≥30 (obesity) kg/mt^2. Arterial hypertension: systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg or use of antihypertensive therapy. Family history of diabetes: father and/or mother suffering or having suffered with diabetes. Physical activity (moderate/intense): <150, ≥150 min/week. Current alcohol consumption: self-reported (never/has quit, not much, a lot). Tobacco consumption: non-smoker (not currently smoking or have smoked no more than 100 cigarettes in their lifetime), former smoker (does not currently smoke but has smoked more than 100 cigarettes in their lifetime), current smoker (currently smoke and have smoked more than 100 cigarettes in their lifetime). Questonnaires were performed in Spanish

Statistical analysis

In order to assess the potential effects of the attrition of the cohort due to non-response, we build a variety of multiple regression models to compare responders with no responders, including various features of the participants and the environment. Such models indicated that no response was not associated with the baseline diabetes diagnoses. Non-responders tended to be male, younger than 45, residents from Lima metro and with more than 12 years of instruction.

To adjust for non-response, we develop a logistic regression model that included the diabetes status, age, sex, level of education, natural region of residence (Lima metro, remaining coast, highlands and jungle) and category of BMI (normal, overweight and obesity). Then, the inverse of the model probability was used to adjust the sampling weights. Several results from the first wave were recalculated using this non-response corrected weights and they yielded consistent results.

For descriptive purposes, we cross tabulated the study variables according to baseline diabetes status using commands for complex surveys to take into account the complex sampling design. For longitudinal estimations, after excluding the prevalent cases, we estimated

the design-weighted cumulative incidence and design-weighted incidence rates per 1000 person-years of follow-up with their corresponding jackknife 95% CI.

To estimate unadjusted and adjusted relative risks (RR), analysis of the predictors of incidence was conducted using design-weighted bivariate and multivariate generalized linear models with robust Poisson distribution and log link. p Values<0.05 were considered significant. All statistical procedures were performed on Stata (V.13).

RESULTS

Forty-five per cent of the study subjects lived in Lima metro (the capital city), 65% were women, 20% were 60 years or older and 36% had technical or higher education. Eighteen per cent had paternal or maternal history of diabetes, 27% were obese and 21% had a previous diagnosis or were in medical treatment for hypertension. The sample distribution according to the baseline diabetes status is shown in table 1.

Diabetes incidence estimates

The cohort was followed for a median time of 3.8 years (min–max: 1.9–4.8). There were 49 cases of diabetes in 2408 person-years follow-up. The design-weighted cumulative incidence (95% CI) and the design-weighted incidence rates were estimated as 7.2 (5.30 to 9.72) per cent and 19.5 (13.9 to 28.3) new cases per 1000 person-years, respectively. Incidence estimates for several subgroups according to the most important predictors reported in the international literature are shown in table 2, along with their RR estimates and corresponding 95% CI.

Predictors of progression to diabetes

In the bivariate analysis, at baseline obesity and being over 60 years old were the strongest predictors of incident diabetes, with risk ratios of 4.14 (1.32 to 13.02) and 9.48 (1.13 to 79.46) compared with people who had normal BMI and those aged between 25–29 years, respectively (table 2). In the multivariate analysis, obesity, being over 44 years old and having technical or higher education (12+ years of study) were independent predictors of incident diabetes.

CONCLUSIONS

To the best of our knowledge, this is the first incidence report of diabetes nationally representative in Peru, and its results place our country among those with the highest incidence reported in the international literature.

Our estimate of incidence (19.5 cases per 1000 person-years) is consistent with population-based estimates of incidence published in 2016 in four areas of three administrative regions of Peru (two on the coast and two in the highlands), using a bigger probability sample than ours (n=3126), that placed the combined incidence of the four communities in 19.5 (16.3–23.3) per 1000 person-years.[9] The sample analyzed in this report is also

Table 1 Baseline characteristics of the population according to the diagnosis of diabetes

Variable	Category	Without diabetes (n=613)	With diabetes (n=49)
Sex	Female	432 (66.6)	33 (52.5)
	Male	181 (33.4)	16 (47.5)
Age (years)	25–44	239 (39.4)	12 (19.6)
	45–64	274 (42.0)	23 (51.9)
	65+	100 (18.6)	14 (28.5)
Formal education (years)	<7	177 (24.4)	18 (22.1)
	7–11	236 (40.6)	10 (25.5)
	12+	200 (35.0)	21 (52.4)
Geographic region	Lima metro	205 (45.6)	16 (43.2)
	Rest of the coast	231 (28.4)	22 (27.9)
	Mountains	129 (20.2)	8 (21.3)
	Rainforest	48 (5.8)	3 (7.6)
Home language	Spanish	600 (97.0)	47 (94.8)
	Quechua	13 (3.0)	2 (5.2)
BMI (kg/mt^2)	<25	197 (31.7)	5 (11.4)
	25 to less than 30	257 (42.2)	20 (46.5)
	30+	159 (26.2)	24 (42.1)
Family history of diabetes	No	503 (82.1)	37 (74.6)
	Yes	103 (17.9)	12 (25.4)
Physical activity	<150 min/week	189 (28.9)	20 (34.4)
	150+ min/week	424 (71.1)	29 (65.6)
Tobacco consumption	Non-smoker	527 (83.1)	42 (85.1)
	Former smoker	39 (6.8)	3 (8.6)
	Current smoker	47 (10.2)	4 (6.2)
Alcohol consumption	Never/Has quit	306 (50.5)	27 (45.3)
	Not much	273 (44.4)	20 (50.7)
	Drinks a lot	34 (5.1)	2 (4.0)
Arterial hypertension	No	493 (78.9)	34 (78.4)
	Yes	120 (21.1)	15 (21.6)

PERUDIAB 2015 Study.
The values in parentheses are percentages weighted by the complex sampling design of the survey. Because of this and the procedure of rounding, some totals may not add up. Rest of the coast refers to all coastal regions and provinces not included in metro Lima. No Smoking: not currently smoking or have smoked no more than 100 in their life. Former smoker: not currently smoking but has smoked more than 100 in their life. Current Smoker: currently smoke and have smoked more than 100 in their life. Arterial hypertension: PAS ≥140 and/or PAD ≥90 mm Hg. BMI, means body mass index.

Table 2 Diabetes incidence rates and unadjusted and adjusted relative risks for predictors of progression to diabetes in Peru

	Incidence per 1000 person-years (95% CI)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Overall (25+ years)	19.5 (13.9 to 28.3)	–	–
Overall (35+ years)	22.4 (15.9 to 32.6)	–	–
Sex			
Female	15.6 (10.6 to 24.1)	Reference	Reference
Male	26.9 (15.3 to 52.1)	1.72 (0.83 to 3.57)	1.54 (0.77 to 3.07)
Age (years)			
25–44	10.2 (5.7 to 20.3)	Reference	Reference
45–64	23.1 (14.4 to 39.5)	**2.26 (1.06 to 4.79)**	**2.57 (1.27 to 6.11)**
65+	29.2 (14.1 to 70.7)	**2.85 (1.12 to 7.26)**	**5.44 (1.80 to 16.42)**
Formal education (years)			
<7	18.4 (10.9 to 33.5)	Reference	Reference
8–11	12.2 (6.0 to 29.1)	0.67 (0.26 to 1.67)	0.94 (0.36 to 2.48)
12+	28.4 (17.2 to 50.4)	1.55 (0.75 to 3.18)	**2.65 (1.18 to 5.96)**
Geographical location			
Lima metro	16.2 (9.3 to 30.8)	Reference	Reference
Rest of the coast	21.6 (13.6 to 36.4)	1.34 (0.68 to 2.64)	1.69 (0.87 to 3.25)
Mountains	23.0 (9.2 to 75.4)	1.42 (0.60 to 3.37)	1.40 (0.62 to 3.15)
Rainforest	31.4 (10.4 to 143.0)	1.94 (0.47 to 8.06)	2.63 (0.60 to 11.66)
Home language			
Spanish	19.1 (13.5 to 27.9)	Reference	Reference
Quechua	30.5 (2.1 to 3671.1)	1.85 (0.76 to 4.46)	1.77 (0.21 to 14.85)
BMI (kg/mt2)			
<25	07.3 (25.0 to 31.3)	Reference	Reference
25 to less than 30	21.4 (12.6 to 39.4)	2.92 (0.90 to 9.44)	2.85 (0.96 to 8.49)
30+	30.3 (18.6 to 52.4)	**4.14 (1.32 to 13.02)**	**4.86 (1.51 to 15.67)**
Family history of diabetes			
No	18.0 (12.3 to 27.5)	Reference	Reference
Yes	27.3 (13.0 to 68.4)	1.52 (0.68 to 3.40)	1.57 (0.81 to 3.04)
Physical activity			
<150 min/week	22.5 (14.1 to 38.1)	Reference	Reference
150+ min/week	18.2 (11.6 to 30.5)	0.80 (0.42 to 1.54)	0.66 (0.36 to 1.21)
Tobacco consumption			
Non-smoker	20.1 (13.8 to 30.3)	Reference	Reference
Former smoker	23.2 (6.9 to 124.8)	1.15 (0.34 to 3.86)	0.58 (0.12 to 2.80)
Current smoker	12.0 (3.6 to 62.0)	0.60 (0.18 to 1.95)	0.46 (0.13 to 1.65)
Alcohol consumption			
Never/has quit	17.5 (10.8 to 30.2)	Reference	Reference
Not much	22.1 (13.4 to 39.5)	1.27 (0.64 to 2.51)	1.25 (0.61 to 2.55)
Drinks a lot	16.2 (3.3 to 168.9)	0.93 (0.22 to 3.85)	0.95 (0.28 to 3.27)
Arterial hypertension			
No	19.4 (12.9 to 30.4)	Reference	Reference
Yes	19.9 (11.3 to 37.8)	**1.02 (0.50 to 2.08)**	0.64 (0.29 to 1.42)

PERUDIAB 2015 Study.
Figures in bold indicate statistically significant values. For incidence estimates, the values in parentheses are jackknife confidence intervals whereas for relative risks they are derived from a bivariate (ie, unadjusted) or multivariate (ie, adjusted) generalized linear model with robust Poisson distribution and log link. No Smoking: not currently smoking or have smoked no more than 100 in their life. Former smoker: not currently smoking but has smoked more than 100 in their life. Current Smoker: currently smoke and have smoked more than 100 in their life.
Arterial hypertension: systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mm Hg.
BMI, means body mass index; RR, relative risks.

a probabilistic one, and includes clusters of all administrative regions (24 regions), distributed in the three natural regions (coast, highlands and jungle), which has a broader representation. Additionally, in order to match our sample age with theirs,[9] we recalculate the Peruvian population incidence for 35+ years as 22.4 (15.9–32.6) cases per 1000 person-years, which is slightly higher than that reported by them, probably because our sample includes the administrative regions with the highest prevalence of overweight and obesity in the country,[11] which are located along the coast of the Pacific Ocean. Our higher figures could also be due to our sample does not include rural areas, but because the rural population is ≈15% of the national population, we believe that its effect weighted as relatively small.

In relation to other countries, our estimates of incidence of diabetes are below those for Indo-Asian population (33.1 per 1000 person-years) in Chennai, India,[6] and the population of Pima Indians (23.5 per 1000 person-years),[12] and would be close to the Chinese population (19.6 per 1000 person-years) living in Ontario, Canada[13] and some ethnic groups living in the USA such as the Korean (20.3 per 1000 person-years) and Pacific Islander (19.9 per 1000 person-years) populations, while our estimate of incidence would be greater than those of Filipino, Native American, Southeast Asian, African American and Latino subgroups, all with incidences between 15 and 10 cases per 1000 person-years.[14] The incidence for Japanese, Chinese, Vietnamese and Caucasian subpopulations living in the USA and estimated at 7.53, 6.5, 6.3 and 4.6 new cases per 1000 person-years, respectively, would also be below our estimates.[14] Another report in the USA, considering all subpopulations, has estimated that between 1980 and 2011, the diabetes incidence for adults aged 18–79 years increased from 3.3 to 6.9 per 1000 person-years, with a peak in 2008 of 8.5 cases per 1000 person-years.[15] In Mexico, it has been reported as 15.8, 15.7 and 12.7 per 1000 person-years for 1994, 1998 and 2008.[16 17]

From here, all published estimates of incidence of diabetes would be below Peru: populations of European descent in Canada (10.0 cases per 1000 person-years),[13] Colombia (8.2 per 1000 person-years),[18] China (8.9 and 9.3 per 1000 person-years, for the period 2013–2014 and for those aged 35–74, respectively),[19 20] Spain (Asturias: 10.8,[21] Lejona 8.0,[22] Madrid: 3.5,[23] Comunidad de Castilla y León: 1.9[24]), Sweden (10.8 and 6.1 per 1000 person-years in 2009 for population of 45–73 year old, male and female, respectively),[25] UK (4.0 and 3.7 per 1000 person-years between 2000–2013, population of 0–99 years, male and female),[26] Scotland (4.9 and 3.3 per 1000 person-years for men and women, respectively),[27] Portuguese population (6.3 per 1000 person-year between 1013 and 2015),[28] United Arab Emirates (4.8 per 1000 person-years, population aged 23–78).[29] Finally, Cuba (2.4 per 1000 person-years)[30] and Denmark, with an estimated 0.6 per 1000 person-years for 2011.[7]

Our study has several limitations. First, it has a small sample size. However, being a probabilistic sample, even at this size should be enough for country estimation, although it may be insufficient for more detailed estimates. Second, the attrition of the cohort is a potential threat. However, analysis of non-response showed that the distribution of the sample was not associated with baseline diagnosis of diabetes; the sample reached all administrative and natural regions of the country, and on the other hand, we used established techniques to compensate for non-response. Third, we did not perform confirmatory Oral Glucose Tolerance Test (OGTT) as required by the American Diabetes Association for clinical purposes[31] and the diagnoses were based on a single glucose test. Therefore, we may have missed some true incident cases, as it has been reported that the OGTT may detect more subjects with diabetes than fasting plasma glucose testing.[32] Also, a detailed review has been published that shows that fasting blood glucose is a reasonable approximation for epidemiological purposes,[33] and we validated the fasting period by protocol, to ensure the concept of unequivocal hyperglycaemia, as required by the American Diabetes Association (ADA).[31] Fourth, we assumed that most of the detected cases were type 2 diabetes, and we did not determine whether they had type 1, 2 or latent autoimmune diabetes in adults (LADA). However, our study participants were all ≥25 years of age, and according to the International Diabetes Foundation (IDF) and an expert review, the prevalence of type 1 diabetes in Peru (0.5 cases per 100 000 population) is one of the lowest in the world.[5 34] No report has been published on LADA frequency in our country.

In our prior study in 2012, the prevalence of diabetes was higher in patients without formal education and in the elderly group. In this present study, young male professionals from the Lima metro area comprised the majority of the non-responder group. However, the non-response analysis, which included the variables of age and years of formal education, among others, showed that neither the diagnosis of diabetes nor those variables were associated with non-response. In addition, the concordance of our results with those of Bernabé-Ortiz et al[9] gives reasonable confidence to our conclusions.

Peru has experienced a strong economic growth in the last 20 years.[35 36] It has been reported to have undergone a nutritional transition,[5] and according to INEI, overweight and obesity rates have increased to 35.5% and 17.8% for those aged 15+ years.[37] More than 3 years ago, a bill was approved by parliament to fight the weight epidemic, but the regulation required to enter in vigor has been delayed to date.[38] Hopefully, our results will hasten the academia and public interest, resulting in renewed efforts to design effective Public Health policies to battle the diabetes pandemic and to avoid an alarming future scenario.

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