Diabetes Mellitus Type 2: Prevalence among men and women in the Peruvian Amazon town of Yantalo

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Abstract:

Objectives: *We will determine the prevalence of type 2 Diabetes Mellitus (DM) and its associated risk factors, in the town of Yantalo.*

Background: *In Peru, the prevalence of type 2 DM in 2014 was 6.1% with an estimated 27.8% of underdiagnosed patients. Knowledge of the disease prevalence outside Lima is very limited, especially in small Amazonian towns such as Yantalo.*

Materials and methods: *A cross-sectional study with two phases, during the first phase participants will be recruited and on the second phase blood will be extracted in order to measure fasting blood sugar, glycosylated hemoglobin (A1C) and lipid profile.*

Limitations: *Geographic accessibility, cultural barriers and the compliance of attendance will be handled.*

Statistical analysis: *A Ratio analysis will be performed to estimate the prevalence of type 2 DM.*

PROBLEM STATEMENT

Type 2 Diabetes mellitus (DM) is a chronic disease that has become a global health problem due to its increasing incidence and impact on morbidity and mortality. It was estimated that in 2000, 150 million people worldwide were living with diabetes, and by 2025, this number will increase to 300 million (1). However, according to the latest report from the International Diabetes Federation (IDF) (2), this calculated number has already been exceeded, reaching up to 387 million people. Of these, 46% have not yet been diagnosed and it is estimated that 77% live in middle and low income countries. Previous studies (3, 4, and 5) have demonstrated the association of this disease with cardiovascular risk factors such as hypertension, obesity and dyslipidemia; increasing disability and mortality.

In Peru, the prevalence of type 2 DM in 2014 was 6.1% (2), which means that approximately about a million and a half of the population were living with the disease. Of these, an estimated 27.8% are underdiagnosed. Particularly, among towns of the Peruvian Amazon there is limited data about the prevalence of DM. Some previous studies (6) have only included large cities but not small towns or rural areas (7).

Thus, our team aims to determine the prevalence of type 2 DM and its associated risk factors in a rural Amazonian town. Our town of choice is Yantalo, located in the San Martin Region, in Northern Peru. We seek to provide current and reliable data in order to develop interventions based on the evidence found.

BACKGROUND

According to the IDF, about 25 million people in central and South America between 20-79 years of age were diabetic in 2014, the overall prevalence in the region

being 8.1%. Because many diabetics have not yet been diagnosed in these countries, efforts regarding adequate screening and arriving at a real approximation of the burden of this disease should be doubled. This issue is reflected in the work of Yang et al, which found that previous studies lacked an appropriate methodology for diagnosing and screening for diabetes (8).

In Peru, there has been limited research into type 2 Diabetes Mellitus, which has nonetheless found differences regarding prevalence according to each region (9-11). In 1999 (7), a type 2 DM prevalence of 4.4% was found in one city of the Amazon region. However, the author used different diagnostic criteria to define DM, which has varied considerably.

Subsequently, according to the Peruvian Society of Cardiology, in the 2004 TORNASOL study, the national prevalence of diabetes was approximately 3.3%. Prevalence by geographic region was determined: 4.3% on the coast (4.5% men and 4.1% women), in the mountains 2.1% (2.4% males and 1.8% females) and in the Amazon 3.9% (3.1% men and 4.6% women), showing statistically significant differences among regions. (7) However, it should be noted that the determination of DM 2 in this study was through surveys, without additional biochemical tests and with a non-probability sampling, so the prevalence reported may be underestimated.

Type 2 DM has multiple associated metabolic risk factors, obesity being the most significant among them. According to the latest update of the American Diabetes Association (12), it is necessary that every patient with a Body Mass Index (BMI) ≥25 kg/m2 should be screen for DM. Therefore, it is alarming that the report of the Nutritional Status in Peru, conducted between 2009 and 2010, showed 42.8% of men and 39.6% of women older than 24 years were overweight. (13)

Other risk factors associated with DM 2 are a sedentary lifestyle, high blood pressure, decreased levels of HDL, high LDL values and some behavior such as alcohol abuse and tobacco consumption.

The above mentioned findings encourage us to discover the characteristics of the type 2 DM and its risk factors in a town from the Peruvian Amazon region, so that measures to reduce the impact and consequences of this disease can be implemented in the future.

JUSTIFICATION

Knowing the prevalence of Diabetes Mellitus 2 and its associated risk factors in Yantalo will allow us to estimate the true burden of this disease. As reviewed, there are few studies in Amazonian regions, and of those conducted, very few have been rigorous in terms of methodology.

Therefore, biochemical diagnostic tests will be included in this study, as well as probabilistic sampling and current diagnostic criteria.

Our work will help to provide suggestions based on evidence, including the prioritization of interventions and the distribution of resources. We hope that in the future, this project will serve as a reference and can be replicated in other towns of the Amazonian region, in order to prevent and mitigate this disease.

FEASIBILITY

Ethical feasibility

The project follows bioethical principles of research involving people; the protocol will be reviewed by the ethics committee of the San Martin de Porres University – School of Medicine (Lima, Peru).

Technical and administrative feasibility

We have the collaboration of trained and qualified personnel to help during the development of this study. The instruments that will be used are in optimal conditions, and the methodology of sampling and conservation of samples perfectly detailed and validated.

Cultural feasibility

Most of the people from Yantalo are well familiarized with the Foundation, which has been providing philanthropic services since 2005. Another advantage of small villages from this region is that dinner is usually served around 6 or 7 pm which will give us up to 10 hours of overnight fasting.

OBJECTIVES

Primary objective

To determine the prevalence of type 2 Diabetes Mellitus and its associated risk factors, in the town of Yantalo.

Secondary objectives

- To identify the association between BMI ranges, waist/hip ratio, and Diabetes Mellitus 2 in the town of Yantalo.
- To identify the association between Blood Pressure and Diabetes Mellitus 2 in the town of Yantalo.
- To identify the association between total cholesterol, HDL cholesterol, triglycerides and LDL cholesterol and Diabetes Mellitus 2 in the town of Yantalo.

- To identify the association between alcoholism, smoking, physical activity and Diabetes Mellitus 2 in the town of Yantalo.

METHODOLOGY

Study design

Cross-sectional.

Target population

Men and women aged 20 to 79 years old from the town of Yantalo.

Sample size

Sample size was determined using the PASS (Power Analysis & Sample Size) version 13 software, and the following assumptions were made:

- Power: 95%
- Study population of 1438 people, which was calculated using an estimate of the total population (20 – 79 years old) by 2015; developed by the National Institute of Statistics and Information (INEI) (15).
- An expected prevalence (P) of 3.9% based on TORNASOL study (7)
- Allowable margin of error (d) of 0.017 (1.7%), because when the expected prevalence is less than 10%, is recommendable to set d= P/2 (16).

Based on the above assumptions, 370 people are needed but considering a 15% of missing data, the final sample size was set to 426 people.

Sampling

A simple random sampling will be performed based on the latest census carried out by the Foundation which includes names and ages of the entire Yantalo population. We will select every men and women between 20 and 79 years old based on a set of random numbers generated from the "Research Randomizer by Geoffrey C. Urbaniak and Scott Plous" software numbered from 1 to 426.

Eligibility

Inclusion criteria

- Every men and women between 20-79 years old, present at the time of data collection in Yantalo in June 2015.
- Person that has been resident of Yantalo for at least six months.
- Person who agrees to participate in the study by signing the informed consent.

Exclusion criteria

- Pregnant Women
- Breastfeeding women
- Person who declined to participate in the study.

STUDY OUTCOME DEFINITIONS

We will follow the guidelines of the American Diabetes Association (12) to diagnose type 2 DM. Results will be categorize as Pre-diabetic (fasting plasma glucose (FPG) ≥110 mg/dl and and <126 mg/dl or A1C 5.7- 6.4%) and Diabetic (FPG ≥ 126mg/dl or an A1C ≥ 6.5 %). Previously diagnosed diabetes will be identified by a positive response from the participant to the question: "Has a doctor ever told you that you have diabetes?". Total diabetic population will include previously diagnosed diabetes and newly diagnosed diabetes. Other variable definitions detailed in Table 1.

PROCEDURES

Prior to the data collection, volunteers for the project will be recruited. They can be medical students from third year or above and general physicians doing their rural service in the San Martin region. They will be contacted by email and will be asked to participate and commit to the project.

Volunteers will be trained by the research team on the correct method of data collection as well as the proper ways to do anthropometric and blood pressure measures.

Recruitment (first week)

- Men and women will be visited at home by the researchers and volunteers according to the sampling list, helped by a local nurse technician who is well familiarized with the neighborhoods.
- It will be determined if the participants meet the eligibility criteria, and then the reasons for the study as well as the process of the informed consent will be explained (Appendix 3).
- People who agree and sign the informed consent will be interviewed according to the questions in the data collection sheet (Appendix 1)
- Participants will have an Identification Number (ID) that will be contained in the data collection and the informed consent sheets, in order to preserve confidentiality.
- Measures such as blood pressure (using a WelchAllyn™ Sphygmomanometer DS44 series with adult cuff and a Littmann™ stethoscope) abdominal and waist circumference (measuring tape in centimeters) will be taken. All this will

VARIABLE	TYPE	CONCEPTUAL DEFINITION	FINAL OUTCOMES	
Gender	NOMINAL	Biological characteristics that define a human being as male or female	Male	
			Female	
Age	NUMERIC	Period of time since the birth of the individual to the day of visit	20 - 39 years	
			40 – 59 years	
			60 - 79 years	
BMI	ORDINAL	Measure of body fat based on height and weight that applies to adult men and women	Low weight:	< 18.5
			Normal:	18.5 - 24.99
			overweight:	greater than or equal 25
			obesity:	greater than or equal 30
			Type II obesity :	greater than or equal35
			Morbid obesity:	greater than or equal 40
BLOOD PRESSURE	ORDINAL	Pressure exerted by circulating blood upon the walls of blood vessels , measure after 10 minutes of rest in semi-supine position.	Normal:	SBP <120 y DBP<80
			prehypertension :	SBP 120-139 o DBP 80-89
			Stage 1 hypertension:	SBP 140-159 o DBP 90-99
			Stage 2 hypertension	SBP ≥160 o DBP ≥100
WAIST CIRCUMFERENCE	NUMERIC	Measure at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest	Pre abdominal obesity and increased risk of comorbidities	Male: ≥ 94 cm
				Female: ≥ 80 cm
			High risk of obesity and comorbidities	Male: ≥102 cm
				Female:≥88 cm
WAIST-HIP INDEX	ORDINAL	Ratio of waist-hip measurements	Male	Low Risk: <0.90
				High Risk:>0.90
			Female	Low Risk: <0.80
				High Risk:>0.80
FASTING PLASMA GLUCOSE	ORDINAL	Measuring glucose levels in 3 ml of venous blood in a patient with a period of at least 8 hours without ingested food.	Diabetes	Fasting serum glucosa ≥ 126mg/dL.
			Pre-diabetes	Fasting serum glucosa ≥100 and < 126mg/dL
			No diabetes	<100 mg/dl
A1C	ORDINAL	Measuring value through biochemical laboratory instument	Diabetes	≥6.5%
			Pre-diabetes	5.7-6.4%
			No diabetes	<5.7%
TOTAL CHOLESTEROL	ORDINAL	Measurement of venous blood cholesterol in a patient with a period of at least nine hours without ingested food	Optimal	<200 mg/dL
			High risk	200-239 mg/dL
			Very high risk	≥240 mg/dL
HDL CHOLESTEROL	NOMINAL	Fraction of high density cholesterol in a patient with a period of at least nine hours without ingested food	Low HDL	< 40 mg/dL in men
				< 50 mg/dL in women
			Optimal HDL	≥ 40 mg/dL in men
				50 mg/dL in women
LDL CHOLESTEROL	ORDINAL	Fraction of low density cholesterol in a patient with a period of at least nine hours without ingested food	Optimal	≤100mg/dL
			almost optimal	100-129mg/dL
			Upper limit	130-159mg/dL
			High	160-189mg/dL
			Very high	≥190mg/dL
TRIGLYCERIDES	ORDINAL	Triglycerides in blood measured in a patient with a period of at least nine hours without ingested food	Normal	<150
			Slightly elevated	150-199
			Elevated	200-499
			Very elevated	>500

Table 1: Variables definitions

comply with international standards of correct measurement of these parameters (14).

- At the end of the visit, participants will be given a card indicating the date and time they must go to the Yantalo clinic (second week).
- The team will emphasize to the population the importance of fasting for 9 to 12 hours before the exam.

Blood sample collection (second week)

- This period will be scheduled from 6 to 11 am at the Yantalo clinic, where blood samples will be drawn from participants.
- Participants will be correctly identified according to their ID given previously.
- Prior to the blood extraction, height and weight (Detecto™ Weigh Beam Eye-Level scale) will be measured.
- Two evacuated blood collection tubes will be filled; one with 3 ml (lavender tube) and the other with 5ml (yellow tube).
- Blood will be drawn from a vein located at the inside of the elbow or the back of the hand by a lab technician using a Safety-Lok™ blood collection set.
- Tubes will be filled until the vacuum is exhausted and blood flow ceases to ensure the proper bloodto-additive ratio.
- It is expected that 40 to 50 samples per day will be collected.
- At the end of the day, the venous blood samples will be processed at the laboratory of the Yantalo Foundation.
- Participants will be instructed to pick up their result a week after.
- Daily processing of blood samples:

65

- All the biochemical tests (glycemia, cholesterol, triglycerides) will be extracted from the yellow (gel and clot) tubes. The samples drawn will be placed in a GeetMed™ Centrifuge GT119-100T for 8 minutes at 4, 000 rev/min. After that, the supernatant plasma will be processed in a WienerLab™ CM 250 auto analyzer.

- Glycosylated Hemoglobin (A1C) will be measured using a Turbidimetric inhibition immunoassay for quantitative determination of A1C. Samples will be drawn from the lavender tubes (10 ul), which will be first processed with a Hemolyzing Re- agent (1000 ul).

Test results

Participants will be able to pick up their results at the Yantalo Foundation confidentially. Abnormal values will be highlighted and a recommendation to visit the local physician will be included.

LIMITATIONS

Geographic accessibility

Yantalo has an average population of 3000 people, who are scattered in the geographic area. However, the feasibility of processing the population's samples has been evaluated, as well as the collaboration with clinic workers according to our schedule.

Compliance of the second visit

The second visit should be early in the morning (6:00 a.m. to 11:00 a.m.) so as to not interfere with participant's daily work routine, and to ensure overnight fasting. Absentees will be contacted and rescheduled within days.

Cultural barriers

People from Yantalo believe that their blood can be sold or they can "dry up" if too much blood is drawn. Another common fear is being sequentially punctured by a needle over short periods of time. Therefore, the team must be very careful in explaining the medical reality and accommodating these fears.

STATISTICAL ANALYSIS

The informed consent sheets and the information collected will be reviewed. Analysis of the Data will be done in STATA 13.0. Continuous variables will be categorized and will be summarized using frequency distributions. To estimate the prevalence of type 2 Diabetes Mellitus in the sample, a ratio analysis will be performed. Paired results (Hb1AC and fasting glucose) will be compared using the Cohen-k value to measure inter-rater reliability in the sample. Chi square test will be used to analyze associations between the outcome and the other risk factors.

Ethical aspects

The study protocol, the data collection sheet and the informed consent was approved by the San Martin de Porres University Ethics Committee on June 3rd 2015 (Appendix 2). We will respect the vital ethical standards in research. The study does not involve any risk to the participants.

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Conflict of interest and financial disclosure

The authors followed the International Committee or Journal of Medical Journals Editors (ICMJE) form for disclosure of potential conflicts of interest. All listed authors concur with the submission of the manuscript, the final version has been approved by all authors. The authors have no financial or personal conflicts of interest.

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