RESEARCH ARTICLE

Diabetes primary prevention program: New insights from data analysis of recruitment period

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Abstract

Background: Primary Prevention of Diabetes Program in Buenos Aires Province evaluates the effectiveness of adopting healthy lifestyle to prevent type 2 diabetes (T2D) in people at high risk of developing it. We aimed to present preliminary data analysis of FINDRISC and laboratory measurements taken during recruitment of people for the Primary Prevention of Diabetes Program in Buenos Aires Province in the cities of La Plata, Berisso, and Ensenada, Argentina.

Methods: People were recruited through population approach (house-to-house survey by FINDRISC in randomized areas) and opportunistic approach (FINDRISC completed by participants during consultations for nonrelated prediabetes/diabetes symptoms in public and private primary care centres of cities involved). In people with FINDRISC score ≥ 13 points, we evaluated blood concentrations of HbA1c, creatinine, lipids, and an oral glucose tolerance test (OGTT).

Results: Approximately 3415 individuals completed the FINDRISC populational survey and 344 the opportunistic survey; 43% of the 2 groups scored over 13 points; 2.8 and 75.4% of them, respectively, took the prescribed OGTT. Approximately 53.7% of the OGTT showed normal values and 5.2% unknown T2D. The remaining cases showed 69.5% impaired fasting glucose, 13.6% impaired glucose tolerance, and 16.9% both impairments. HbA1c values showed significant differences compared with normal glucose tolerance (4.96 ± 0.43%), prediabetes (5.28 ± 0.51%), and T2D (5.60 ± 0.51%). Participants with prediabetes showed a predominant increase in low-density lipoprotein-cholesterol values. In prediabetes, >50% showed insulin resistance.

Conclusions: People with prediabetes/T2D had dyslipidemia associated with insulin resistance, which promotes the development of T2D and cardiovascular disease. Thus, it merits its appropriate treatment.

KEYWORDS
diabetes primary prevention, dyslipidemia in prediabetes, FINDRISC score, prediabetes

1 | INTRODUCTION

Diabetes prevalence in Argentina grew from 8.4 to 9.8% between 2005 and 2013, mainly conditioned by type 2 diabetes (T2D). The frequent association of T2D with other cardiovascular risk factors facilitates development/progression of chronic complications responsible for their high morbidity and mortality and economic cost. Type 2 diabetes develops in people with genetic predisposition exposed to unhealthy diets and physical inactivity; therefore, adoption of healthy lifestyles is the most effective way to prevent the disease, a concept supported by the successful reduction, up to 58%, of T2D development through implementation of primary prevention programmes in different countries and ethnic groups. Based on such experience, there is a strong European movement towards promoting diabetes prevention programme implementation.
in their region that even has developed a tool kit to use for that purpose.\textsuperscript{6} Despite strong evidence of the preventive effectiveness of lifestyle changes in people at high risk of developing T2D, before implementing such programmes at national level, it is necessary to verify how they work in our environment, identify potential difficulties/barriers to preventive goals to avoid or neutralize them, and estimate the programme’s cost.

Consequently, and given the lack of national evidence, we initiated the Pilot Program for Primary Prevention of Diabetes of Buenos Aires Province (PPDBA), aiming to evaluate the effectiveness of healthy lifestyle adoption on the clinical manifestation of T2D in people at increased risk of developing the disease. This report shows preliminary analysis of data obtained during recruitment of people for the PPDBA in 3 cities of Buenos Aires province.

2 MATERIALS AND METHODS

The characteristics of the PPDBA were previously reported.\textsuperscript{7} Briefly, it is a prospective, randomized cohort study to evaluate the benefits of adopting healthy lifestyles (healthy meal plan and regular practice of physical activity) on the transition from prediabetes (impaired glucose tolerance [IGT], impaired fasting glycaemia [IFG], or both) to T2D. This study recruits men and women between 45 and 75 years of age with prediabetes according to the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD)\textsuperscript{8} in 3 municipalities of Buenos Aires province (La Plata, Berisso, and Ensenada). For recruitment, we used 2 different procedures:

1. **Populational approach**: We randomly selected census areas in each municipality as explained in the previous publication;\textsuperscript{7} in these areas, previously trained students of the last year of the School of Medicine of La Plata National University visited homes to administer the Finnish Diabetes Risk Score (FINDRISC).\textsuperscript{9}

2. **Opportunistic approach**: This scheme was used previously for prediabetes and cardiovascular risk factor detection\textsuperscript{10}; in our case, people visiting a physician’s office for reasons other than prediabetes/diabetes filled out the FINDRISC. To facilitate this approach, we invited physicians in primary care centres of the participant municipalities and in private groups in La Plata. Consequently, the sample included persons from both public health and social security sectors.

In both approaches, people with a FINDRISC score \( \geq 13 \) points (cut-off value indicated by Prof Jakko Tuomilho, PPDBA advisor) were invited to receive free of charge an oral glucose tolerance test (OGTT) following WHO recommendations.\textsuperscript{11} In the OGTT fasting blood sample, we also measured concentrations of HbA1c (by high-performance liquid chromatography technique), creatinine, total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, and triglyceride by using commercial kits. All blood samples were processed in a single laboratory (CentraLab, CABA, Argentina) within 24 hours after extraction.

People with normal glucose tolerance (NGT) were advised to repeat the OGTT in 1 year, whereas those with a diagnosis of T2D were referred to their own physician for appropriate treatment. Those who presented prediabetes (IFG, IGT, or both) and met the PPDBA inclusion criteria were invited to participate in the PPDBA after acceptance and signing of the informed consent. Thereafter, these people were randomly assigned to one of our 2 study groups (intensified and self-administered intervention) as previously reported.\textsuperscript{7}

2.1 Ethical issue

The study protocol was analysed and approved by the Bioethical Committee of the National University of La Plata and the Central Ethics Committee of the Ministry of Health of the province of Buenos Aires. The study was developed according to the Good Practice Recommendations (International Harmonization Conference) and the ethical guidelines of the Helsinki Declaration. All subjects gave their written informed consent to participate in the study, and this was signed before blood samples were collected.

2.2 Statistical analysis

With the FINDRISC and laboratory data collected during the early recruitment period (2014-2015), a descriptive and inferential statistical analysis was performed by using SPSS (Statistical Package for Social Sciences), version 15.0 for Windows (SPSS Inc, Chicago, IL, USA). Continuous variables are presented as means and standard deviations and categorical variables as proportions. Differences in continuous variables were assessed by using parametric and nonparametric tests according to the normal distribution of the variables (Kolmogorov-Smirnoff test), using the \( \chi^2 \) test to evaluate the differences in proportions. Differences with \( P \) values <.05 were considered significant.

3 RESULTS

Finnish Diabetes Risk Score: 3415 questionnaires were completed with the populational approach and 344 with the opportunistic one. Their results showed a normal distribution with 43% of participants scoring \( \geq 13 \) points; 23% and 3%, respectively, had high and very high scores of risk (FINDRISC criteria)\textsuperscript{9} of developing T2D (Figure 1). Whereas in the populational approach, only 2.8% of people prescribed the OGTT did it, 75.4% of people in the opportunistic approach in the same condition took the OGTT.

Comparing FINDRISC results from people below and above 13 points, we found an asymmetric percentage distribution of each of the 8 questions within the 2 groups: people in the latter group had a higher percentage of physical inactivity, medication taken to control blood pressure, age (were older), BMI corresponding to overweight/obesity, waist circumference above the normal cut-off value, low daily consumption of fruits and vegetables, and history of hyperglycaemia.

The largest percentage corresponded to waist circumference (81%) and physical inactivity (74%), while history of hyperglycaemia was recorded only in 20% of the this group.
According to the OGTT results and cut-off values suggested by the ADA-EASD, our sample included 3 categories of people: (1) with NGT, (2) with prediabetes (IFG/IGT or both), and (3) with undiagnosed/untreated T2D (Figure 2). Although we only prescribed OGTT for people with a score ≥ 13, 53.7% of them showed normal results.

Figure 2 also shows that 5.2% of the individuals evaluated had unknown/undiagnosed and consequently untreated T2D. Further data analysis showed that in 63% of cases of T2D and in 62% of prediabetes identified, diagnosis was based on the fasting blood glucose value of the OGTT.

HbA1c values recorded to date showed significant differences when comparing the 3 following groups: people with NGT (4.96 ± 0.43%), with prediabetes (5.28 ± 0.51%), and with T2D (5.60 ± 0.51%; Figure 3). Participants with prediabetes and T2D showed a similar abnormal lipid profile characterized by total cholesterol, LDL-c, and triglyceride levels above those recommended by international guidelines (Table 1). Increased LDL-c levels were the most frequently detected change in the prediabetes group, this frequency comparable with that observed in people with T2D.

We did not measure insulinaemia; therefore, we have no direct indicator of insulin resistance (IR) in people with prediabetes. We instead used 2 indirect measures: a clinical (waist circumference) and a laboratory test (triglyceride/HDL-c ratio) using cut-off values validated in our population. According to waist circumference (men > 102 and women > 88 cm), 78% of participants with prediabetes had IR, whereas that figure was 51% for the triglyceride/HDL-c ratio (values >3.5 and >2.5 for men and women, respectively). Thus, independent of the index applied, more than half of our prediabetes population displayed IR.

4 | DISCUSSION

Current PPDBA data show barriers to the participants’ recruitment, evidence of diabetes diagnostic inefficiency in our care system, and some novel data.

While the FINDRISC data show similar results for the 2 collection approaches, adherence to OGTT prescription was significantly higher with the opportunistic approach (75.4 vs 2.8%). Adherence failure could be attributed to (a) subjectively “healthy” persons reject the diagnosis of a serious but asymptomatic disease after a medical student asked 8 questions; (b) inadequate population and health system promotion of preventive practices considering the absence of symptoms (especially pain); and (c) the subjective inclination to follow their physician’s prescriptions more readily than those of an unfamiliar health agent. Therefore, the opportunistic rather than the populational approach is more advisable for use in similar studies implemented in our culture.

Finnish Diabetes Risk Score, with low cost and easy performance, decreased the prescription of OGTT (57%), thereby optimizing resources. Although the weakness of this assumption is that the
FINDRISC has not yet been validated in our local population, it has been used in Caucasian, Spanish, and other Latin American populations; these studies also yielded data comparable with those currently recorded. In any case, the cut-off value currently used rendered 53.7% of normal OGTT; thus, it would require an adaptation of this value to our population to optimize outcomes. This assumption is supported by some European authors’ conclusions that the FINDRISC is currently the best available tool for use in clinical practice being, the FINDRISC with its current score is still a useful and effective tool at the primary care level.

Another important aspect of our FINDRISC data analysis is that family history of diabetes, which represents the effect of inheritance of prediabetes/T2D development, is reported by people at high risk in a markedly lower proportion than waist circumference, blood pressure, and frequency of dyslipidemia and metabolic modulators released by physical activity. These data support the concept that epigenetic alterations facilitate the development of prediabetes and its progression to T2D.

The 3 different prediabetes stages identified by OGTT (IFG, IGT, and both) have a different annual transition rate to T2D: 12% for the third stage and 4 and 6% for the other 2, respectively. Therefore, the implementation of preventive strategies is correspondingly more or less imperative. In our case, most people with dysglycaemia presented IFG (69.5%); a finding also reported by other authors who showed that these people have significantly larger values of waist circumference, blood pressure, and frequency of dyslipidemia and cardiovascular disease (CVD). It has been also reported that they have already lost 50% of their β-cell mass. Thus, when planning to implement a primary prevention intervention and having low availability of human and economic resource, systematic measurement of fasting blood glucose might be an incomplete but still reasonable approach to identify people with prediabetes.

Using the sequence FINDRISC-OGTT, we identified 5% of people with T2D who were unaware of their disease and untreated; these results could suggest the advisability of systematic prescription of OGTT for diabetes detection. However, 63% of people with undiagnosed with T2D and 62% of those with prediabetes were identified by fasting glycaemia values. Therefore, ongoing awareness of health care team members concerning the importance of careful analysis of fasting blood glucose values by searching for diagnostic values recommended by national and international guidelines could overcome the problem. The importance of this awareness is further supported by the report that late diagnosis increases the risk of cardiovascular morbidity and mortality more than late treatment.

Based on the recommendations of the Experts Committee convened by ADA, EASD, and International Diabetes Federation to redefine diabetes diagnosis by HbA1c values, different countries established their own cut-off values for prediabetes and T2D diagnosis. Current HbA1c values result from the first local study of this type.

Participants with prediabetes and T2D displayed similar dyslipidemia characterized by abnormal changes in all lipid fractions; an increase in the LDL-c fraction was the most frequently detected, indicating a high risk for developing atherosclerotic CVD. Thus, prediabetes stage is a risk for developing T2D but also for CVD. Because we found no marked differences between the frequency of increased LDL-c in people with prediabetes and T2D, its presence in the former stage could be more a cause than a consequence of β-cell dysfunction. Identification of plasma lipoprotein receptor in pancreatic β cells involved in their binding/processing and the report that LDL particles reduce insulin mRNA levels and β-cell proliferation and induce a dose-dependent increase in their apoptotic rate support this assumption. Conversely, HDL-c particles antagonize the proapoptotic effect of LDL-c. Therefore, the deleterious effect of increased LDL-c on β-cell function/mass could be potentiated by the simultaneous decrease in HDL-c concentration.

Finally, using 2 indirect measurements (waist circumference and TG/HDL-c ratio), we demonstrated that most people with prediabetes have IR.

We recognize that although our evidence is clear, it is based on certain circumstances and on a low number of cases. However, its...
statistical significance suggests that it is unlikely to be the result of chance.

In conclusion, early results of PPDBA implementation demonstrate that (1) sequential performance of FINDRISC-OGTT is an effective strategy to identify people with prediabetes or T2D who were unaware of their disease; (2) people with prediabetes present a state of IR associated with dyslipidemia that favours development of T2D and CVD; thus, this is a stage of disease rather than predisease stage that merits its immediate treatment; (3) in our media, and probably in other ones with similar socioeconomic characteristics, the opportunistic approach implemented through primary care physicians was a more effective strategy to identify people with prediabetes; (4) health authorities must be aware of prediabetes and T2D underestimation occurring at the primary care level to correct this deficiency; and (5) final PPDBA data will more accurately define national HbA1c cut-off values for prediabetes and T2D diagnosis. Our data contribute to develop effective strategies to decrease the diabetes burden.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest related to this project.

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