Systems Nutrology of Persons with Tuberculosis Identifies Specific Dietary Profiles Associated with Dysglycemia

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Research Article

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Abstract

Objective: Dietary pattern may be associated with overall nutritional status that can alter the risk of tuberculosis (TB) disease. This complex interaction can be further intricated by additional metabolic comorbidities such as dysglycemia (diabetes or prediabetes). This study aimed at identifying dietary pattern associated with dysglycemia in TB patients.

Research Methods & Procedures: A prospective cohort study of TB patients and their household contacts was conducted between February and November 2017 in Lima, Peru. Among the 269 patients, 85 were considered healthy, 48 had dysglycemia, 75 had TB and 61 had TB-dysglycemia. Food intake was collected using a food frequency questionnaire and a Systems Nutrology analytical approach was employed to identify dietary pattern associated with these groups. Potential associations between clinical factors and dietary pattern were also analyzed.

Results: Three dietary patterns were identified based on the food intake profile of the study participants. Normoglycemic TB patients more often had the dietary pattern 1, while healthy individuals more frequently presented with the dietary pattern 2 and persons with TB-dysglycemia were more represented in the dietary pattern 3.

Conclusion: TB-dysglycemia was mainly associated with the increased intakes of rice and cereals, fast food and oils. The identification of distinct dietary patterns involved with TB and dysglycemia may help to guide nutritional interventions to optimize patient care.

Background

Tuberculosis (TB) is one of the top ten causes of death in worldwide [1], although most deaths could be prevented with early diagnosis and appropriate treatment. Globally, around 10 million people fall ill with TB, with more than 1.45 deaths annually [2]. The combination of TB with other diseases affects the control, clinical severity, and treatment response [3, 4]. The co-occurrence of diabetes mellitus (DM) in persons with TB is thought to be related with more extensive lesions in the lungs [5], with a risk 3.9 times of higher treatment failure [6] and a higher risk to develop multi-drug resistance TB (MDR-TB) [7].

In Peru, there were around of 28,892 new TB cases in 2019, of which 11.5% also had dysglycemia (i.e. with either DM or prediabetes) [8]. This proportion of TB patients with dysglycemia could contribute to the increased risk of treatment failure and high burden of MDR-TB [1] noted in Peru, and warrants investigation of potential determinants of adverse outcomes in those with TB and DM, including the role of diet.

Several studies have assessed the relationship of dietary intake with risk of TB disease [9], and separately with diabetes. For example, higher intake of milk and dairy, green vegetables, fruit and berries has been associated with a reduced risk of diabetes mellitus (DM) [2,3]. In addition, other studies have reported the variation of the body mass index (BMI) among TB patients, before, during and at the end of TB treatment [10] and the underweight as a high risk factor for TB-specific and non-TB-specific mortality during anti-TB treatment [11]. There is also evidence that vitamin D [12] and vitamin A [13] concentrations in peripheral blood could affect the incidence and progression of TB. However, there is a gap in the literature about the evaluation of dietary patterns in the comorbid condition of TB and DM, and on whether such information may be useful to guide optimization of clinical management.

Following World Health Organization (WHO) guidelines, the Peruvian national TB program covers the full cost of TB treatment and offers psychological and nutritional counseling. Additionally, the program provides food baskets monthly to all patients in treatment through the Food and Nutrition Program for Outpatients with Tuberculosis and Family [14–16]. This provision of food baskets is offered to increase treatment adherence, improving weight gain and reduce mortality [14]. However, the increased frequency of patients with TB-DM comorbidity [15] raises the question of whether the current nutritional recommendations are appropriate. In a previous study, our group used big data and artificial intelligence analysis tools to develop the concept of Systems Nutrology, in order to identify dietary profiles of populations based on unsupervised analyses [16, 17]. Such knowledge and approach may be useful to define nuances in the dietary profiles that may be associated with dysglycemia in persons with TB. The present study employed our Systems Nutrology approach to characterize dietary patterns in individuals with TB and dysglycemia in a cohort of persons with TB enrolled in Lima, Peru.

Methods

Study design

This cross-sectional study is part of a prospective cohort study of pulmonary TB patients and their household contacts, conducted between February and November 2017 in Lima, Peru, which was main aimed to determinate the prevalence of DM and prediabetes (preDM) in persons with TB. The study was carried out in the Public Hospital Sergio Bernales and outpatient health centers of Carabayllo and Comas districts. Patients with pulmonary TB with ≥18 years of age diagnosed by the Peruvian National TB Program, who are not receiving anti-TB treatment or have started it in a period of no more than 5 days, were included. Exclusion criteria were patients or contacts diagnosed with HIV, pregnant women, who did not live permanently in the jurisdiction area of the study and patients who had infection or disease due to non-tuberculous mycobacteria. The follow-up of those patients and household contact was conducted up to 6 to 12 months after enrollment. 136 TB patients and 133 household contact were included in this study and classified in the investigated groups (dysglycemia, TB and TB-dysglycemia) and the control group, with healthy patients.

Furthermore, for this study we use the information from the TB patients and their contacts collected at the baseline visit (before the TB patient initiates anti-TB treatment). Clinical and epidemiological information (such as: age, sex, prior TB, among others) was used for analysis, in addition to the laboratorial results of hemoglobin (Hb), glycated hemoglobin (HbA1c), oral glucose tolerance test (OGTT) and fasting plasma glucose (FPG).

The recruitment details, laboratory and field procedures were described in the previous study of our group with the same cohort [15].

Definitions

TB patients were diagnosed according to definitions of the Peruvian National TB Program [18] in the health centers, by one or more of the following criteria: (a) clinical factors (presumptive diagnosis), (b) bacteriology (sputum smear positive) or positive culture (solid or liquid), (c) GeneXpert MTB RIF, and (d) chest radiography). Household contact was defined as a person who shared at least household where they sleep or take their meals (at least one of them per day) with a study TB patient.

DM was defined in agreement with American Diabetes Association (ADA) guidelines [19] as 2h OGTT≥200 mg/dL, HbA1c ≥6.5% or FPG ≥126 mg/dL. PreDM was also defined in agreement with ADA guidelines as 2h glucose 140 a 199 mg/dL, HbA1c 5.7 - 6.4% or fasting plasma glucose 100–125 mg/dL. Dysglycemia was defined as DM or PreDM.

Healthy controls were participants that did not have dysglycemia or TB diagnosis. Anemia was defined following WHO criteria as Hb levels below 12.5 g/dL and 13.5 g/dL for female and male patients, respectively. Hb measurement was performed in whole blood specimens stored at – 80 °C from patients approximately one year after the blood sample collection at the end of the enrollment. One 50 µL-aliquot of whole blood of each participant was thawed and separated in a new tube to be passed through the HumaCount 5D Hematology System (Wiesbaden, Germany). In our cohort, there are a good proportion of TB-dysglycemia people that are anemic. There is evidence supporting the idea that performance of HbA1c in detecting dysglycemia is affected by occurrence of anemia. Our previous study found no clear influence in the HbA1c test performance to diagnose DM and showed that FPG is indeed a good marker to be used for screening of DM or pre-DM in Peru.

Anthropometric status was defined according to the body mass index (BMI). The different anthropometric statuses were defined according to the conventional WHO classification: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2) [20].

Food Consumption data collection

The food intake was obtained according to a food frequency questionnaire (FFQ), with 94 food items. FFQ was specifically developed for this study, to delineate the dietary patterns of TB patients and household contacts, with and without dysglycemia. In addition, the data retrieve and processing of variables were performed following standardized steps from a previous study from our group [16, 17]

The FFQ was applied to TB cases and their household contacts at the enrollment visit (before the patient initiated anti-TB treatment). The consults about the habitual diet were referred to consumption of food outside and inside the home in the last 6 months. The food frequency choices had the following response options: Never / rare; 1 to 3 times a month; 1 time per week; 2 to 4 times a week; ≥4 times a week. In addition, the number of times you consumed these foods was investigated. After data collection, through the use of food composition and nutrition tables, we standardized the amounts consumed of each food and / or preparation referred to units of weight (g) and / or volume (mL), which w[i]ere used for calculating the daily consumption of the food recorded in the FFQ. Industrialized foods and / or preparations that were not included in the tables were searched through the internet directly on the manufacturer's website or through recipes. Thus, it was possible to obtain an approximation of the total daily food consumption in grams through calculations based on weekly and monthly consumption.

The average of daily consumption in grams of these food items were provided by the self-report of participants. For the statistical analysis, the food items that composed the FFQ were categorized into 10 food groups according to the similarity in nutritional composition and food habits of the Peruvian population: Sugar and sweets, sweetened beverages, tubers, fast food, oils, milk and dairy, fruits and vegetables, rice and cereals, meat, and legumes. The approach used for creating these groups is described below (**Table 1**).

Statistical Analysis

Comparison between groups

Characteristics of study participants were presented as median and interquartile ranges (IQR) for continuous variables or frequency for categorical variables. Continuous variables were compared using the Mann-Whitney *U* test (between two groups) or Kruskal-Wallis test with Dunn's multiple comparisons. Categorical variables were compared using the Fisher's exact test (2 × 2 comparisons) or Pearson's chi square test. For comparisons of abundance of food consumption, the one-way ANOVA was used. Categorical variables were displayed as frequency (%) and compared using the Pearson's chi-square test.

Systems Nutrology Analysis

To analyze the potential association between food consumption profiles, anthropometric and dysglycemia status, we used an analytical approach denominated 'systems nutrology', created and detailed by our group in the article of Andrade et al. (2020), based on ecological analysis approach [21, 22].

Hierarchical cluster analysis

To evaluate the overall profile of consumption of the different food groups, we transformed data on total consumption of each food group (in grams) into abundance of consumption relative to total diet. This is a common method used in ecological analysis and was used previously by our group evaluating food consumption of humans [16, 17]. After defining the proportion of consumption of each food group in the total ingestion we performed an unsupervised hierarchical cluster analysis to define the dietary patterns (Ward's method). Individuals were grouped based on similarity of abundance of food consumption. The different clusters were defined by overall similarity of food consumption, represented using dendrograms denoting the Euclidean distances. We also used bubble plots to illustrate the representativeness of consumption of each food group in each one of the food patterns calculated, using three measurements: low, middle, and high. Pie charts were used to illustrate frequency of individuals grouped by clinical group, sex, and anemia status in each dietary pattern.

Correlation between foodgroups and glucose levels

Correlations between total intake in grams of each food group and clinical variables associated to glucose levels (HbA1c and FPG) were evaluated by the Spearman rank test. We created correlation matrices stratifying the participants according to TB status. A correlation was considered to be weak with values below 0.45, moderately strong when the value of rho was between 0.45 and 0.75 and above 0.75 to be relatively strong.

Multinomial logistic Regression

To test the association between the clinical groups and the different dietary patterns identified (n=3) in the hierarchical cluster analysis, we performed a multinomial multivariate logistic regression analysis, adjusted for age, sex, hemoglobin and BMI. As in a previous study of our group [17], the outcome variable was the pattern of food consumption. The dietary pattern 2 was used as the baseline for estimation of odds of consumption of the other patterns, given that most patients in this cluster are healthy.

Prespecification and used software

All analyses and data visualization were pre-specified. Two-sided P value < 0.05 after adjustment for multiple comparisons (Bonferroni's method) were considered statistically significant. Statistical analyses were performed using R 3.4.2 (R Foundation) and SPSS 24.0 (IBM statistics). The R packages corresponding to each analysis are described in **Supplementary Table 1**.

Results

Study population and characteristics

Our cohort was composed of 269 patients from Lima, Peru. The patients were firstly grouped according to TB and DM status and all characteristics are described in **Table 2**. Among the patients in the study, 85 (31.59%) were considered healthy, 48 (17.84%) had dysglycemia, 75 (27.88%) had TB and 61 (22.67%) had TB and dysglycemia. The median age was highest for patients with dysglycemia at 50.6 years (IQR: 40.2-61.0), while TB patients had the lowest median age with 25.8 years (IQR: 21.3-31) ($p<0.001$). In the present study, there were 137 men and 132 women, however the frequencies of males in the investigated groups (dysglycemia, TB and TB-dysglycemia) were higher than females. In the control group, with healthy patients, this proportion was inverse ($p = 0.002$).

Besides the lower proportion of males, healthy patients also had lower frequency of use of cannabis, illicit drugs and alcohol, as well as lower levels of HbA1c (4.90, IQR: 4.60-5.20). Dysglycemic patients presented lowest frequencies of anemia and higher values of BMI (29.6, IQR: 27.9-33.3), waist circumference (98.0, IQR: 93.8-106), hemoglobin (13.6, IQR: 12.8-14.2), FPG (106, IQR: 102 – 114) and HbA1c (5.30, IQR: 4.90 - 5.73). TB patients showed the highest percentage of males (62.7%), a higher frequency of illiteracy and cannabis use. In contrast, TB patients presented lower values of BMI, waist circumference and glucose. TB dysglycemia group presented the lowest frequency of illiteracy (9.84%) and higher frequencies of illicit drugs and alcohol use and anemia, as well the lowest level of hemoglobin (11.4, IQR: 10.2 - 12.6) (**Table 2**).

Food intake between clinical groups

In comparisons of food group intake (grams per day), we observed statistical differences for all the food groups between the clinical groups, with $p < 0.001$ (**Table 1**). Healthy patients had lower intakes of rice and cereals and sweet potato, and higher intakes of legumes, fruits and vegetables compared to the other groups. Dysglycemia group had lower intakes of legumes and higher intakes of meat, and milk and dairy. TB patients presented the lowest total consumption of all foods, with lowest intakes of milk and dairy, fruits and vegetables, meat, fast food, sugar and sweets and oils. Finally, TB-dysglycemia group presented the highest total consumptions, with higher intakes of rice and cereals, sweet potato, fast food, sweetened beverages, sugar and sweets and oils (**Table 3)**.

Dietary patterns associated with TB-Dysglycemia

An unsupervised hierarchical cluster analysis (Ward’s method) was used to identify dietary patterns of the consumption of distinct food groups, independent of the study group (Healthy, dysglycemia, TB and TB-Dysglycemia). It was possible to identify three dietary patterns (DP), with 104, 74 and 91 patients, respectively (**Supplementary Table 2**). While analyzing the dietary patterns according to the relative abundance of the food groups consumed, it was possible to observe that rice and cereals was the most representative food group in all three clusters, followed by sweet potato (**Figure 1A**). However, comparing the groups with each other we observed that DP1 exhibited the highest intakes of these food groups and also the highest frequency of persons with anemia (**Supplementary Table 2 and 3**). In contrast, DP2, that presented with the highest frequency of females ($p<0.001$), displayed higher intakes of fruits and vegetables, legumes, and meat, while DP3 presented the highest intakes of sweetened beverages, fast food and milk (**Figure 1B, Supplementary Table 2 and 3**).

Additional analyses tried to test associations between the dietary patterns and the clinical groups. All TB patients (with and without dysglycemia) were distributed in DP1 and DP3, while none of patients at DP2 presented this pathology ($p < 0.001$). In general, DP1 was predominantly composed by TB patients without dysglycemia (68.3%), with the youngest median age (26.4, IQR: 21-37, $p <0.001$), highest frequency of illiteracy (32.7%, $p = 0.002$), cannabis use (12.5%, $p = 0.008$) and anemia (59.6%, $p<0.001$). In contrast, the patients in this DP also presented lowest values of BMI (22.3, IQR: 20.2-24.5, $p < 0.001$), waist circumference (79.5, IQR: 74-87.2, $p < 0.001$) and HbA1c levels (5, IQR: 4.7-5.3, $p < 0.001$). DP3 was composed mainly for patients with dysglycemia with and without TB (94.5%, being 63.7% with TB, $p <0.001$), with the elderly median age (45.9, IQR: 30.5-54, $p <0.001$), highest illicit drug use (11%, $p <0.005$), fasting plasma glucose (104, IQR: 99-114, $p <0.001$) and glycated hemoglobin (5.3, IQR: 4.9-5.9, $p<0.001$). Finally, at DP2 are allocated almost all healthy patients (89.2%, $p <0.001$), with a small frequency of males (33.8%, $p = 0.002$), without illicit drug or cannabis use reported, highest BMI (27.4, IQR: 25.3-30.1, $p <0.001$), waist circumference (90, IQR: 83.2-98.8, $p <0.001$) and hemoglobin levels (13.1, IQR: 12.4-14.2, $p=0.014$) (**Figure 2 and Supplementary Table 3**).

To evaluate the influence of the intake of food groups on the glycemic status of the study participants (assessed here through FPG and HbA1c levels), we performed a Spearman correlation test between these two variables and each food group, stratifying the patients according to TB status. In our cohort, we observed that there was a higher correlation between some food groups and FPG in both groups (**Figure 3A, Supplementary Table 4**), but no statistically significant correlation was observed with glycated hemoglobin values (**Figure 3B, Supplementary Table 4**). In patients without TB, consumption of rice and cereals and sweet potato was positivity correlated with FPG levels while that of Legumes was negatively correlated. In TB patients, besides the consumption of rice and cereals, that of fast food and oils was also positively correlated with FPG levels (**Figure 3, Supplementary Table 4**).

Association between clinical characteristics and dietary patterns

To test for independent association between the DP identified and the clinical groups, we performed a multinomial multivariate logistic regression analysis, as described in Methods. We used DP2 as reference and tested the associations between clinical and epidemiologic characteristics and DP1 and DP3 (**Figure 4**). Using this approach, we found that obesity (adjusted Odds Ratio [aOR]: 1.02, 95%CI: 1.01-1.40, $p = 0.028$) and dysglycemia status (aOR: 1.88, 95%CI: 1.44-7.69, $p < 0.001$) were associated with DP1 independent of other tested factor. On the other hand, overweight (aOR: 1.70, 95%CI: 1.31-2.20, $p<0.001$), TB-Dysglycemia comorbidity (aOR: 4.92, 95%CI: 1.53-9.23, $p<0.001$) and dysglycemia condition (aOR: 1.16, 95%CI: 1.01-7.99, $p= 0.047$) were independently associated with the dietary pattern 3.

Discussion

It is common knowledge that there is a synergism between nutrition and the development of several human pathologies [23], which can be applied to diabetes [24] and tuberculosis [13]. In 2013, the guideline of Nutritional care and support for patients with tuberculosis was published [8]. TB and poor nutritional scenario are commonly recognized as associated because either of them can be a risk of the other [25]. It has been established that poor nutritional status is associated with limited cellular immunity (key for host defense against TB) and increased susceptibility to infections [26]. On the other hand, changes in eating behaviors and other factors have been related to the prevalence of diabetes in a scenario whose global trend towards obesity is widely distributed and documented in many regions of the world [27]. Moreover, the infection leads to nutritional stress and weight loss, thus weakening immune function and nutritional status [28] which could favor the development of other syndromic status.

In Peru, rice is the basis of the diet, and according to the Peruvian Ministry of Agriculture, rice consumption has grown by 25% between 2001 and 2009 [29]. That is why the consumption of rice in the study population, both in patients affected with TB and in those affected with the comorbidity TB-Dysglycemia, is high, as is the consumption of tubers (for example potatoes) and some other cereals. Potato intake was commonly associated with an increased risk of diabetes, through a mechanism related to increased glucose levels, although the glycemic index of the potato depends largely on the strain and the method used in preparation [30]. Because of this popular knowledge, may the population with dysglycemia avoid this type of food, justifying the lowest levels in DP3. On the other hand, as tuberculosis is often associated with worse nutritional status, it is expected that the intake of foods rich in carbohydrates such as potatoes will be stimulated in this population, as can be seen in DP1. It is remarkable to find that health directions recommend consuming foods rich in complex carbohydrates such as potatoes, sweet potatoes, rice, wheat and cereals [31]

In may setting such as that observed in Peru, malnutrition is due to excess to the consumption of foods with high energy content and low nutritional value, with the growing popularity of junk food, not expensive and ready to be eaten at any time. These new eating patterns have caused different health issues. Ultra-processed foods are really preferred in the Peruvian population and although various messages have appeared to avoid the use of some beverages, especially sodas or carbonated drinks, so-called fruit juices bottled together with sources of starch, are widely preferred and diverted by a bad message, little time for the preparation of better drinks and low economic possibility to avoid them [32]

Studying the patterns of food consumption is key to knowing the food system available as a manifestation of the functioning of food and in turn, they determine the nutritional status and especially the health of the population. Characterizing the composition and heterogeneity of the diet, especially in patients with the comorbidity TB-dysglycemia, will help us to understand the relationship with the low rates of therapeutic success in little-explored considerations and with this it will be possible to design policies aimed at promoting a healthy state of life. The eating patterns of Latin countries have traditionally been marked by a strong presence of foods based on cereals, roots and tubers. At the country level, a great heterogeneity is observed in the proportion of the availability of dietary energy derived from said foods and in Peru estimates indicate that they contribute half of the energy diet. New eating patterns, together with less physical activity and unhealthy lifestyle habits, currently contribute to the accelerated increase in the levels of chronic non-communicable diseases such as dysglycemia or diabetes, obesity, among others; that affect an increased risk of Tuberculosis, among other infectious problems and death. The worst thing about this is that the treatment of comorbid conditions will have increasing impacts on the development of countries and on the sustainability of public health systems and national budgets [33].

With this systems nutrology analysis we found that aging was associated with DP3, mostly formed by individuals with TB-dysglycemia comorbidity. Previous studies have described how increasing age alters glucose metabolism [34]. In addition we identified that the highest BMI values were in DP2, where the consumption of fruits, vegetables, meat and legumes was higher than in the other two DPs, in addition to grouping more to healthy individuals and multinomial analysis confirms that the obesity condition was more associated with DP2, while overweight condition was associated with DP3, this is reported in previous findings in Singapore [35], where there were no differences between BMI and dysglycemia status among TB patients.

This study has limitations. In the first place, it has been difficult to have a wide range of socioeconomic data in enrolled patients to evaluate the relationship between economic power and dietary pattern. Certain disproportions have been assumed in the affected people, since normally the TB problem is as widespread in Lima as poverty, unemployment, malnutrition, and lack of access to an effective health system. On the other hand, the study could not use a specific form to evaluate eating patterns. Standardized surveys are not available to health professionals linked to the work of the TB prevention and control strategy, and this study has been carried out mainly under programmatic conditions. Finally, given that Lima concentrates more than two thirds of the TB and diabetes problem; the study was carried out only, in an urban population. Although the centralization in Lima and the consequent migration, allows an extrapolation of the customs still rooted in the population, it is possible that we can only represent a percentage of what happens in all of Lima or the country.

Conclusions

The new trends towards responsible consumption practices constitute an opportunity to promote public policies and multi-stakeholder agreements to promote transformations in current health systems. These changes should promote healthy lifestyles in the population; For this reason, it is necessary to innovate and implement policies in different areas, which are aimed especially at the most vulnerable population that, due to various socioeconomic factors, does not have access to food in sufficient quantity, quality, and variety.

Abbreviations

ADA	American Diabetes Association

ANOVA	Analysis of variance
BMI	Body Mass Index
DM	Diabetes mellitus
DP	Dietary patterns
FFQ	Food frequency questionnaire
FPG	Fasting Plasma Glucose
Hb	Hemoglobin
HbA1c	Glycated hemoglobin
HIV	Human immunodeficiency virus
IQR	Interquartile ranges
MDR-TB	Multi-drug resistance tuberculosis
OGTT	Oral glucose tolerance test
preDM	Prediabetes
TB	Tuberculosis
WHO	World Health Organization

Declarations

Ethics statement

The study was approved by the Institutional Committee of Ethics for Humans (CIEI, approval number: 158–22–16) of the Universidad Peruana Cayetano Heredia, with the authorization of National Institute of Health in Peru. Written informed consent was obtained from all participants or their legally responsible guardians, and all clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki and local and national Peruvian regulations.

Consent for publication

Not applicable.

Availability of Data and Materials

All data containing relevant information to support the study findings are provided in the manuscript.

Competing of Interest

The authors declare no conflict of interest.

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Author Contributions

Conceptualization, MBA, VBA, RS, LL and RIC; Data curation, MBA, MA-P, VBA, CDF, JA and RIC; Formal analysis, MBA, MA-P, CDF and CS; Investigation, MBA, MA-P, VBA, CDF, CS, JA, RS, LL and RIC; Project administration, LL and RIC; Resources, LL; Supervision, LL, RIC and BBA; Validation, MBA and MA-P; Visualization, MA-P; Writing – original draft, MBA, MA-P, CDF, RS, RIC and BBA; Writing – review & editing, MBA, MA-P and BBA.

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Tables

Table 1. Food groups according to similarity in nutritional composition, consumed by adolescents enrolled in the study.

Food or Food Group	Food Items
Rice and cereals	Bread (white or whole), rice (white or whole), noodles (white or whole), flour, oats, green corn or couscous of corn, popcorn salted, homemade cake, biscuit (salted or sweet), pasta soup, picarones[a], wheat, quinoa.
Tubers	Cassava, sweet potato, potato, yucca, *ullucus*[b].
Milk and dairy	Whole milk powder or liquid, skimmed milk powder or liquid, yogurt (whole, diet or light), chocolate ready, yellow cheese, white cheese.
Fruits and Vegetables	Lettuce, cabbage, pumpkin, squash, carrot, tomato, chayote, gherkin, beet, okra, vegetable salad, pineapple, avocado, silver banana, ground banana, cashew, papaya, mango, apple, watermelon, melon, orange, tangerine, strawberry, fruit juice or fruit pulp, lettuce, cucumber.
Legumes	Beans, lentils, chickpeas, pallares[c].
Meat	Bovine (fried or cooked), chicken with or without skin (fried or cooked), cooked or fried fish, seafood, viscera, chicken egg (fried or cooked), dehydrated meat (Jerky beef).
Fast Food	Fried potatoes, potato chips, pizza, lasagna, ketchup, ready-made soups, sandwich, industrialized salty snack, instant noodles, ready-to-eat sauce and pizza-ready sauce, salty potato.
Sweetened beverages	Normal, diet or light soda, artificial juice, carbonated drinks, artificial refreshment, tea, coffee, energy drink and liquid or powdered sweetener.
Sugar and sweets	Sugar, chocolate powder, homemade sweets, industrialized sweets, stuffed biscuit, candies, chewing gum, lollipops, chocolate bar, gelatin, ice cream and popsicle (cream and/or chocolate) and flan[d].
Oils	Butter and vegetable oil.

Table Note: [a]Picarones: Peruvian dessert based in squash and sweet potato. [b]Ullucus: a plant grown primarily as a root vegetable, secondarily as a leaf vegetable. [c]Pallares: Peruvian beans. [d]Flan: is a dessert made-up of eggs and milk with a soft caramel on top

Table 2. Characteristics of the study population according TB and dysglycemia status.

Parameter	Healthy	Dysglycemia	TB	TB-Dysglycemia	
	n=85	n=48	n=75	n=61	P value
Age (years), median (IQR)	31.0 (19.8 - 44.2)	50.6 (40.2 - 61.0)	25.8 (21.3 - 31.0)	43.3 (29.7 - 53.9)	<0.001
Male, n. (%)	29 (34.1)	25 (52.1)	47 (62.7)	36 (59.0)	0.002
Illiteracy, n. (%)	18 (21.2)	7 (14.6)	28 (37.3)	6 (9.84)	0.001
Prior TB, n. (%)	9 (10.6)	5 (10.4)	10 (13.3)	13 (21.3)	0.249
Smoking, n. (%)	12 (14.1)	7 (14.6)	15 (20.0)	14 (23.3)	0.455
Passive smoking, n. (%)	11 (12.9)	8 (16.7)	5 (6.67)	6 (10.0)	0.342
Cannabis use, n. (%)	0 (0.00)	2 (4.17)	13 (17.3)	8 (13.3)	<0.001
Illicit drug use, n. (%)	0 (0.00)	1 (2.08)	8 (10.7)	9 (15.0)	<0.001
Alcohol use, n. (%)	24 (28.2)	24 (50.0)	37 (49.3)	33 (55.0)	0.004
Anemia, n. (%)	32 (37.6)	10 (20.8)	49 (66.2)	50 (82.0)	<0.001
BMI (kg/m^2), median (IQR)	26.1 (22.9 - 29.4)	29.6 (27.9 - 33.3)	22.3 (20.4 - 25.2)	23.0 (21.5 - 25.7)	<0.001
Waist (cm), median (IQR)	88.0 (79.0 - 94.0)	98.0 (93.8 - 106)	80.0 (74.0 - 86.0)	84.0 (78.0 - 89.0)	<0.001
Hb (g/dL), median (IQR)	13.2 (12.2 - 14.2)	13.6 (12.8 - 14.2)	12.6 (11.2 - 13.4)	11.4 (10.2 - 12.6)	<0.001
FPG (g/dL), median (IQR)	90.6 (87.5 - 94.1)	106 (102 - 114)	89.9 (85.8 - 94.6)	104 (99.8 - 136)	<0.001
HbA1c (%), median (IQR)	4.90 (4.60 - 5.20)	5.30 (4.90 - 5.73)	5.00 (4.70 - 5.20)	5.60 (5.10 - 6.75)	<0.001

Table Note: The data presented in continuous variables (represented median and interquartile range [IQR]) between clinical groups were compared using the Kruskal-Wallis test with Dunn’s multiple comparisons post-test. Qualitative variables were represented by number and frequency (%) and compared using the

Pearson's chi-square test. P-values were adjusted for multiple measurements using the Holm-Bonferroni method.

TB: tuberculosis; TB TMG: tuberculosis and dysglycemia; BMI: body mass index; Hb: Hemoglobin; HbA1c: glycated hemoglobin.

Table 3. Food group consumption per grams according TB and dysglycemia status.

Food group (g/day)	Healthy	Dysglycemia	TB	TB Dysglycemia	p-value
	n=85	n=48	n=75	n=61	
Total consumption	1046 (963 - 1225)	1232 (1160-1350)	981 (885-1095)	1616 (1459-1733)	<0.001
Rice and cereals	490 (474 - 506)	574 (567 - 594)	559 (430 - 565)	645 (615 - 651)	<0.001
Tubers	187 (175 - 191)	237 (233 - 247)	233 (163 - 233)	275 (268 - 278)	<0.001
Milk and dairy	69.3 (34.7 - 107)	139 (69.3 - 213)	34.7 (34.7 - 61.3)	88.0 (42.7 - 213)	<0.001
Fruits and Vegetables	52.0 (34.7 - 78.0)	34.7 (26.0 - 62.8)	8.67 (8.67 - 13.0)	13.0 (13.0 - 21.7)	<0.001
Legumes	45.5 (31.5 - 49.0)	14.0 (14.0 - 17.5)	17.5 (10.5 - 21.0)	17.5 (10.5 - 21.0)	<0.001
Meat	50.3 (35.5 - 67.3)	56.6 (41.0 - 70.8)	33.0 (25.0 - 40.0)	42.2 (29.7 - 53.3)	<0.001
Fast Food	60.7 (28.3 - 74.7)	59.3 (51.3 - 108)	53.7 (18.7 - 74.7)	216 (123 - 427)	<0.001
Sweetened beverages	33.3 (33.3 - 83.3)	33.3 (6.25 - 133)	33.3 (8.33 - 83.3)	233 (100 - 267)	<0.001
Sugar and sweets	20.0 (20.0 - 20.0)	20.0 (10.0 - 25.0)	15.0 (10.0 - 20.0)	40.0 (20.0 - 45.0)	<0.001
Oils	5.33 (2.67 - 8.00)	10.7 (7.67 - 21.3)	2.67 (2.67 - 5.33)	10.7 (6.67 - 21.3)	<0.001

Figures

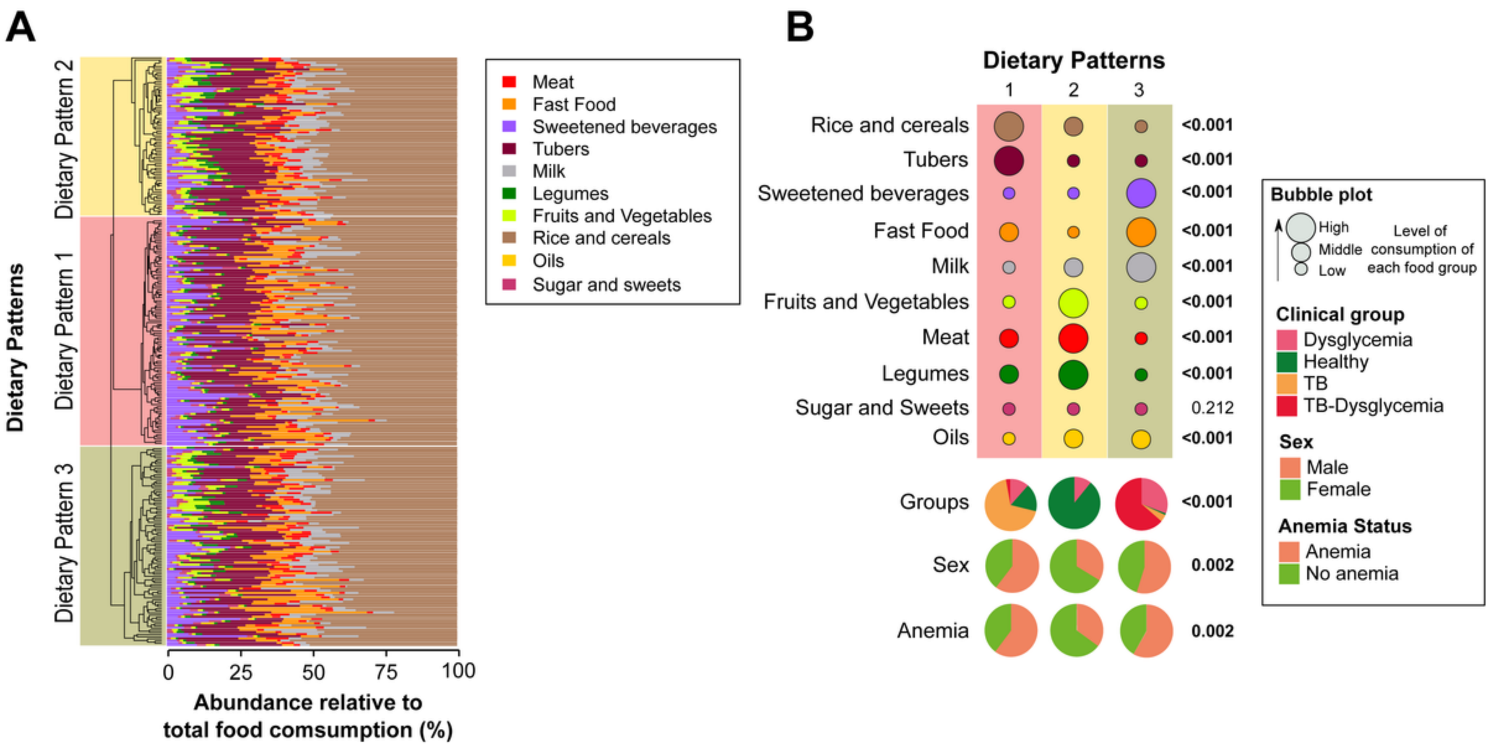

Figure 1

Dietary patterns of food groups using hierarchical clustering. The abundance of consumption of the indicated food groups in the diet was calculated for each one as described in Methods. (A) Hierarchical cluster analysis using Ward's unsupervised method. The dendrograms represent the Euclidean distance and was used to identify different consumption profiles. Using this approach, it was possible to identify three major dietary patterns. (B) Upper panel shows the abundance consumption stratified in high, middle and low, of each food group within each dietary pattern identified in the hierarchical cluster analysis. Lower panel shows frequencies individuals in each dietary pattern stratified by clinical groups, sex and anemia. To calculate the p-values, the average relative abundance of consumption of each food group was compared between the different dietary patterns using two-tailed one-way ANOVA. Proportions of clinical groups, sex and anemia were compared between the different dietary profiles using the Pearson's chi-square test. All p-values are indicated. The values of these analysis are detailed in Supplementary Table 2 and 3. Abbreviatures: TB: Tuberculosis.

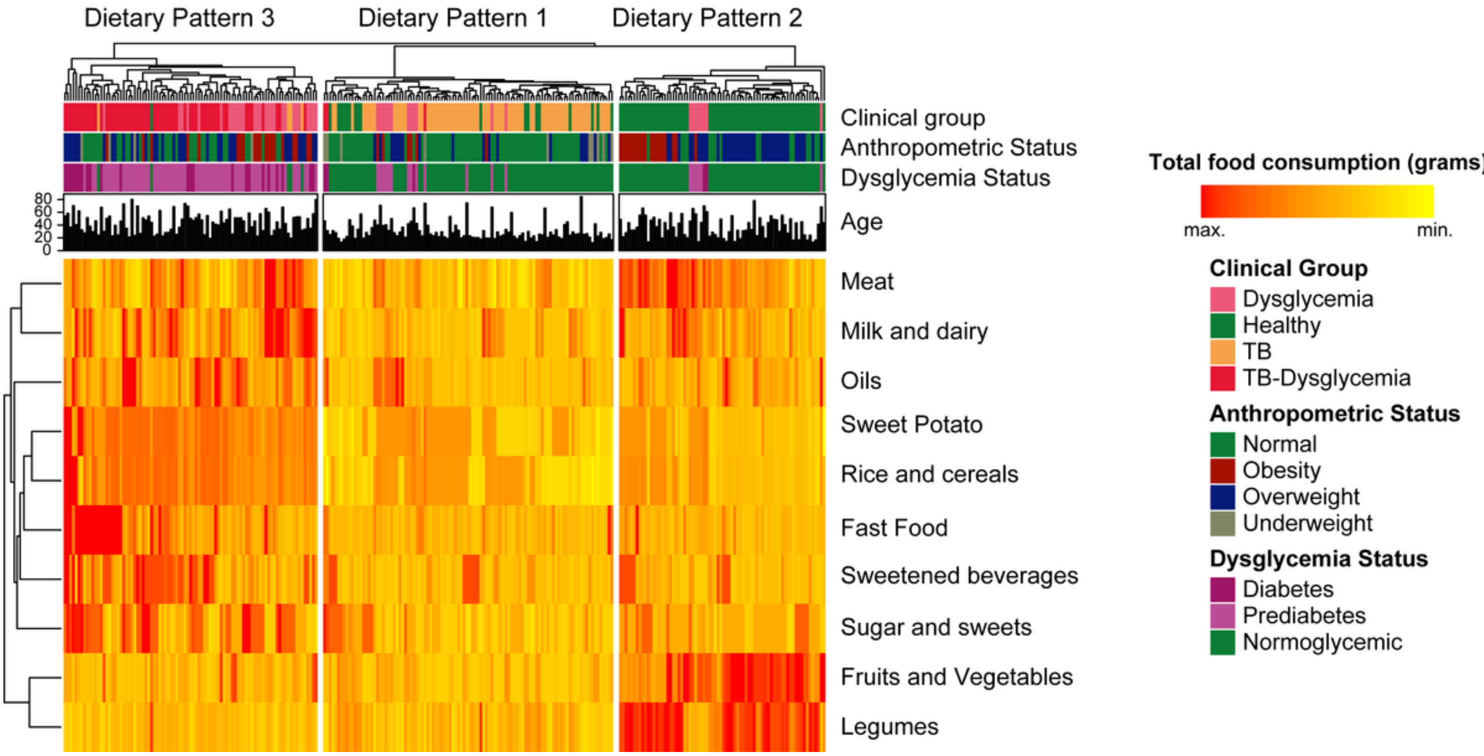

Figure 2

Analysis of the consumption of dietary groups using hierarchical cluster. The total consumption in grams obtained for each food group was calculated. Two-way hierarchical cluster analysis (Ward's method, unsupervised), in which the dendrogram represent Euclidean distance, was used as an approach to identify similarity profile of the consumption of distinct food groups. Using this approach, it was possible to identify three clusters of study participants that exhibited similar patterns of consumption in the general population. Information about group, anthropometric status, diabetes mellitus and are exhibited above the heatmap. Abbreviatures: TB: Tuberculosis

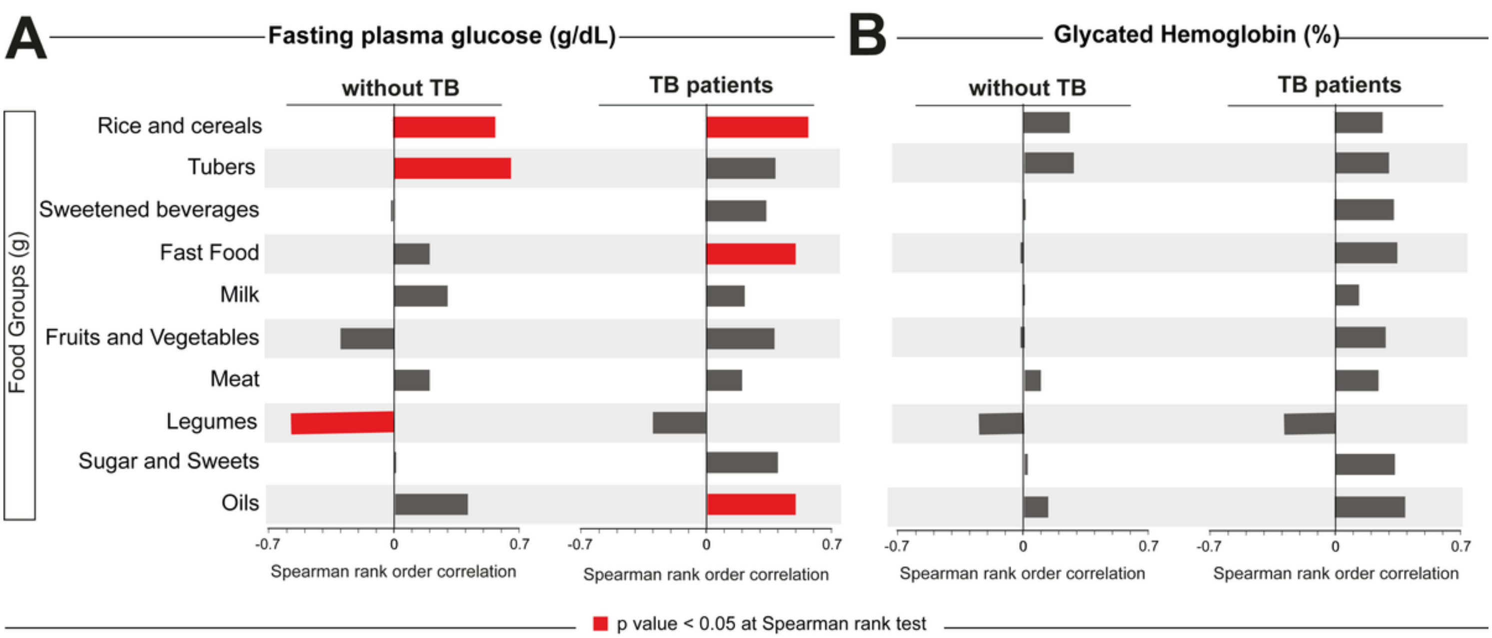

Figure 3

Correlations between food consumption and values of FPG and HbA1c. A Spearman correlation test was performed between Fasting plasma glucose (A) or Glycate Hemoglobin (B) versus total consumption in grams of each food group. Significative correlations (|rho| > 0.45 and p < 0.05) for each glycemic test and group are highlighted in red bars. The values of these analysis are detailed in Supplementary Table 4. Abbreviatures: TB: tuberculosis.

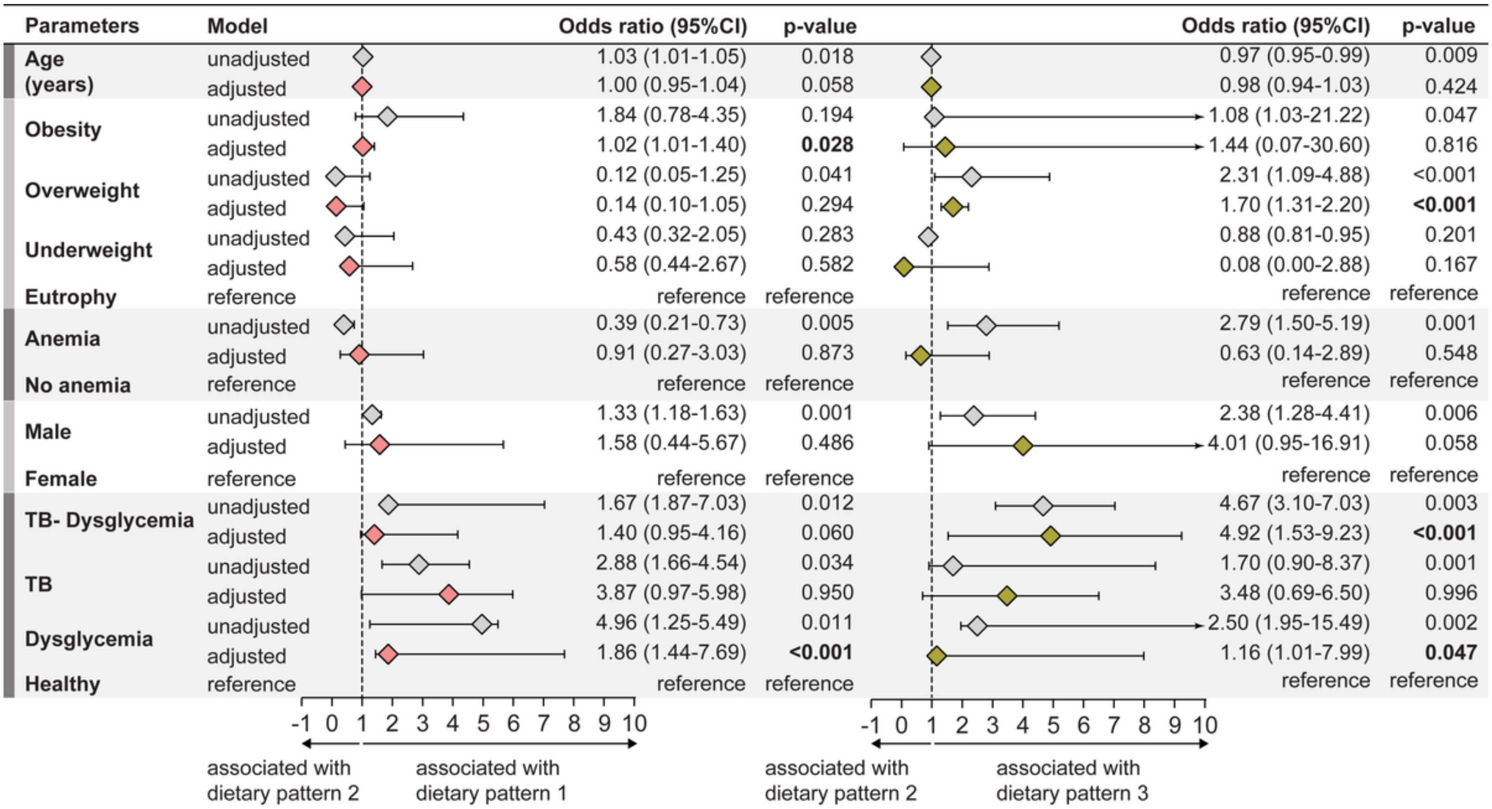

Figure 4

Multinomial logistic regression to test independent associations with the dietary patterns. Adjustment was performed for all variables presented in the figure. The dietary pattern 2 profile was used as reference to test associations between variables and dietary pattern 1 and 3. The statistical significance was estimated through a multinomial logistic regression model. The values of these analysis are detailed in Supplementary Table 2. Abbreviatures: TB: tuberculosis, CI: Confidence interval.

Supplementary Files

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