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Research Article

Prediabetic patients evaluated with Quantose™ IR and their relationship with anthropometric measurements through bioelectrical impedance analysis

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ABSTRACT

Introduction: New metabolomic biomarkers as Quantose™ IR and anthropometric measurements using bioelectrical impedance analysis (BIA) provide relevant information on patients with insulin resistance and prediabetes. Quantose™ IR is a novel metabolomic test to assess insulin resistance for screening and monitoring. Establishing a correlation between these variables is useful in clinical practice and, to our knowledge, there are no published studies that explore the relationship between Quantose™ IR and anthropometric measurements using BIA in patients with prediabetes. **Objective**: To evaluate the correlation between Quantose™ IR and BIA anthropometric variables (fat mass, FM; fat mass index, FMI; and body mass index, BMI) in Mexican patients with prediabetes, overweight, and obesity. **Materials and Methods**: This is an observational, transversal analytic study in 135 patients of both genders between 20 and 65 years of age, BMI 25.0–34.9, with diagnosis of prediabetes. The Quantose™ IR test was performed as well as anthropometric measurements (FM, FMI, and BMI) using BIA taken with Inbody 230™. Pearson's correlations and independent sample t-tests were estimated with a significance level of $p < 0.05$. **Results**: 135 patients were studied; 77% were female, aged 46 years in average. The prevalence of insulin resistance by Quantose™ IR was 71.1%. A positive correlation was confirmed between Quantose™ IR and FM, FMI, and BMI ($p < 0.05$). Patients with altered Quantose™ IR had higher FM, FMI, and BMI ($p < 0.05$). **Conclusion**: The data here presented confirm the existence of a positive and statistically significant correlation between Quantose™ IR and anthropometric measurements using BIA. This information may be useful for diagnosis and treatment in prediabetic, overweight, and obese patients.

Key words: prediabetes; Quantose™ IR; bioelectrical impedance analysis; fat mass; fat mass index; BMI.

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RESUMEN

Introducción: Los nuevos biomarcadores metabolómicos, como el Quantose^{MR} RI y las medidas antropométricas por bioimpedancia eléctrica (BE), aportan información importante sobre los pacientes con resistencia a la insulina y prediabetes. La nueva prueba de metabolómica, Quantose^{MR} RI mide resistencia a la insulina para escrutinio y monitoreo. No se identifican estudios sobre la relación entre Quantose^{MR} RI y variables antropométricas de BE en pacientes con prediabetes y consideramos que establecer una correlación entre ellos es de utilidad en la práctica clínica. **Objetivo**: Evaluar la correlación entre Quantose^{MR} RI y variables antropométricas de BE (masa grasa (MG), índice de masa grasa (IMG) e índice de masa corporal (IMC) en pacientes mexicanos con prediabetes, sobrepeso y obesidad. **Materiales y Métodos**: Estudio observacional, transversal-analítico en 135 pacientes entre 20 y 65 años de edad, ambos géneros, IMC 25.0–34.9 y diagnóstico de prediabetes. Se realizaron prueba Quantose^{MR} RI y mediciones antropométricas de MG, IMG e IMC por BE, Inbody 230^{MR}. Se estimaron correlaciones de Pearson y prueba t-Student para muestras independientes. El nivel de significancia fue $p < 0.05$. **Resultados**: Se estudiaron 135 pacientes; 77% de ellos, mujeres con edad promedio de 46 años. La prevalencia de resistencia a la insulina por Quantose^{MR} RI fue 71.1%. Se confirma correlación positiva de Quantose^{MR} RI con MG, IMG e IMC ($p < 0.05$). Los pacientes con Quantose^{MR} RI alterada tienen MG, IMG e IMC superiores ($p < 0.05$). **Conclusión**: Los datos aquí presentados confirman una correlación positiva y estadísticamente significativa entre Quantose^{MR} RI e indicadores antropométricos por BE. Esto es de utilidad para el diagnóstico y tratamiento en pacientes con prediabetes, sobrepeso y obesidad.

Palabras clave: prediabetes; Quantose^{MR} RI; bioimpedancia eléctrica; masa grasa; índice de masa grasa; IMC.

INTRODUCTION

Currently, an epidemiological emergency has been declared for type 2 diabetes, overweight, and obesity in several countries, including Mexico.[1] In 2013, the global prevalence of prediabetes was between 15 and 25%.[2] In Mexican adults the rate is even higher, at 43.2%.[3] Some of the main causes of the rise in prediabetes are the growing rate of overweight and obesity and the delay in identifying risk factors that can be prevented.[1] Consequently, the early diagnosis of prediabetes becomes essential to slow the progression of and prevent type 2 diabetes and its complications.

The most frequently used biomarkers for diagnosing prediabetes are glucose and fasting serum insulin, homeostatic model assessment of insulin resistance (HOMA-IR), HbA1c, postprandial glucose, and oral glucose tolerance test. Recently, new biomarkers associated to insulin resistance (IR) and prediabetes have been developed.[4] Among these biomarkers, the Quantose™ IR test was developed through metabolomic studies and validated with the clamp technique. It is now used in different clinical settings in the Mexican population. The main advantage of Quantose^{TM} IR is the ease with which it measures insulin resistance before glycemic changes in one blood sample. Within this context, Quantose^{TM} IR allows clinicians to obtain a picture of intracellular analytes using an algorithmic analysis to identify insulin resistance.[5]

The implementation of the Quantose™ IR test can facilitate an early diagnosis and the possibility of establishing timely treatment strategies to promote long-term benefits. This is supported by the observation of altered insulin functionality (insulin resistance) up to 5 years before presenting symptomatology suggestive of prediabetes or type 2 diabetes. The Quantose™ IR test consists of the analysis of three metabolites: hydroxybutyric acid (α-HB), Linoleoylglycerophosphocholine (L-GPC), and oleic acid. All three play an important role in metabolic routes related to the action and secretion of insulin or beta cell function. In their Relationship between Insulin Sensitivity and Cardiovascular Disease (RISC) Study, Cobb et al. validated the Quantose™ IR test to measure insulin resistance. Then they predicted the risk of progression to impaired fasting glucose within three years. Fasting plasma levels of α-HB, L-GCP, oleic acid, and insulin significantly correlated with glucose stimulated by insulin.[5-6]

Additionally, the analysis of anthropometric measurements using bioelectrical impedance analysis (BIA) provides useful data for clinical practice, which can be correlated with metabolomic biomarkers.

Compared to the body mass index (BMI), fat mass (FM) correlates more precisely with health risk factors. BMI does not measure body composition. Conversely, FM and fat mass index (FMI) provide information about excess fat. FMI is more specific than BMI because it takes fat mass into account instead of body weight, which is composed of fat mass and fat-free mass constituents. It is useful to detect abnormalities in body composition and to establish reference criteria to estimate prevalence rates of obesity or sarcopenia in clinical studies.[7]

It is known that increased body mass and FM, as determined by BIA, are risk factors of insulin resistance and prediabetes.[8,9] The early identification of insulin resistance among these patients is crucial. Until now, no studies have explored the relationship between the Quantose™ IR test and anthropometric

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measurements, using BIA in prediabetic patients. Thus, it is of interest to conduct an analysis of these parameters to define prediabetic patients' characteristics.

The aim of the current study is to evaluate the correlation between metabolomic biomarkers (Quantose™ IR) and anthropometric measurements (FM, FMI, and BMI) in Mexican patients with prediabetes, overweight, and obesity.

MATERIALS AND METHODS

The study design was observational and transversal-analytical. The study was conducted in a primary care clinic between 2019 and 2020 and included 135 patients between 20 and 65 years of age with BMI of 25.0–34.9 and prediabetes diagnosis (American Diabetes Association criteria).[10] The patients showed glycated hemoglobin (HbA1c) levels of 5.7–6.4%, impaired fasting glucose of 100–125 mg/dL, or glucose intolerance of 140–199 mg/dL, with or without hypertension and/or dyslipidemia with medical management and no pharmacological treatment for prediabetes. Patients with medically uncontrolled comorbidities (i.e., cardiovascular diseases, chronic kidney disease, thyroid disease, adrenal disease, or liver disease), pregnant or breastfeeding females, and those with dehydration were excluded. Follow-up visits were scheduled with their physicians.

In accordance with the World Medical Association Declaration of Helsinki, the study was approved by the Research and Ethics Committees of the ABC Medical Center, (approval number ID ABC-17-13). Patients accepted participating in the study after they were explained the procedure and read and signed their informed consent.

For this study, the sample size required to estimate a proportion with an accuracy of 5% determined for $\alpha = 0.05$. The expected proportion of insulin resistance was 86.9%. The study by Vatcheva et al. (2020) was used as reference.[8]

Serum sample measurements. Quantose™ IR is a metabolomic test using bioanalytical strategies. The techniques used are mass spectroscopy and ultra-high performance liquid chromatography. Both identify and determine a set of metabolites and biomarkers highly discriminatory in biological diseases.[11] This test was conducted with a fasting blood sample. Blood samples were taken in a supine position after 10 h of fasting, confirmed verbally by patients. Medical laboratory technicians drew the samples at the laboratory of the ABC Medical Center. The laboratory is accredited by the College of American Pathologists (CAP). Quantose™ IR is given within a 1–120 range, where higher scores indicate more insulin resistance. When the value of Quantose™ IR was equal or higher than 63, the presence of insulin resistance was defined.[5-6]

Height and weight were measured with 0.5 cm and 0.1 kg precision using a BIA Inbody 230™ scale and a SECA 206™ wall-mounted stadiometer. FM was obtained from the BIA analyzer in absolute (kg) and relative (%) value. FMI and BMI were obtained from estimations with FM (kg), weight (kg), and height (m). After having been previously standardized, measurements were taken by the nutritionists.[12] Measurements were conducted on patients wearing disposable gowns after 4 h of fasting.

BIA is based on determining body volume, resistance to current, the distance covered by an electrical impulse, and body surface dimensions. BIA measures extracellular liquid and total body water when exposed to low and high electric frequency. FM does not conduct electric charge and is equal to the difference between body weight and fat-free mass. Fat-free mass is considered the conducting volume that helps an electric current impulse to travel thanks to the conductivity of electrolytes dissolved in body water. BIA measurements are obtained from the entire body and body segments using four electrodes, one on each limb.[13]

To conduct the BIA, subjects were placed in the center of the scale freely (without holding onto anything) and with equal weight distribution on both feet. The stretch stature method required that the subject stand with feet together and heels, buttocks, and upper back against the stadiometer. The head was supported on the Frankfort Plane without touching the stadiometer. The measurement was taken at the end of a long exhalation.[12]

FM was classified as obesity when the relative value was ≥ 25 and ≥ 32 for men and women.[14] The FMI was calculated dividing FM (kg) by the squared height (m). An excess fat or obesity due to FMI was defined by values > 9 and > 13 for all patients.[7] BMI was calculated dividing the weight (kg) by the squared height (m). BMI criteria were defined by the WHO. The value of ≥ 25 defined overweight and ≥ 30, obesity.[15] FM (kg), FMI (m/ kg^2), and BMI (m/ kg^2) were analyzed as continuous quantitative variables.

Statistical analysis

The qualitative and quantitative variables of the patients were calculated through frequencies and proportions and mean and standard deviation (SD). The prevalence of insulin resistance was estimated with Quantose™ IR. FM, FMI, and BMI were presented with means and SD. Pearson's correlations were obtained to measure the relationship between Quantose™ IR and FM, FMI, and BMI. T-tests for independent samples were conducted to compare the means of FM, FMI and BMI between groups, with and without alteration in the Quantose™ IR test. The significance level was determined with a value of $p < 0.05$. A statistical analysis was conducted with SPSS v 27.

RESULTS

The study sample consisted of 135 patients. Table 1 shows descriptive information with demographic and clinical variables. Of the total sample, 77% were female and the mean age was 46 (± 8.3) years. Average FM was 31.1 (± 8.3), indicating FM obesity. Average FMI was 12.7 (± 3.7) kg/m^2, indicating excess fat or obesity. BMI was 30.7 (± 4.0) kg/m^2, indicating obesity as well.

TABLE 1. Description of demographic and clinical variables of study sample (n = 135).

	Frequency	%
Female	104	77
Age, mean, and SD	46.0	8.3
FM (%), mean, and SD	31.1	8.3
FMI (m/kg^2), mean, and SD	12.7	3.7
BMI (m/kg^2), mean, and SD	30.7	4.0

FM: Fat mass. FMI: Fat mass index. BMI: Body mass index.

Figure 1 shows the prevalence of insulin resistance (71.1%) measured by Quantose™ IR. Figure 2–4 show the correlations between Quantose™ IR and FM (%), FMI (m/kg^2), and BMI (m/kg^2). Positive and statistically significant correlations were found between insulin resistance measured by Quantose™ IR and body mass and FM composition measured by BIA.

Table 2 shows the mean comparison of FM, FMI and BMI and the presence of insulin resistance measured by Quantose™ IR. Patients with altered Quantose™ IR had higher FM (%), FMI (m/kg^2), and BMI (m/kg^2) means than those with unaltered Quantose™ IR. Mean differences were statistically significant.

Based on our observations, it is suggested that the biomarker Quantose™ IR is positively correlated and statistically significant with anthropometric BIA parameters that indicate body fat composition.

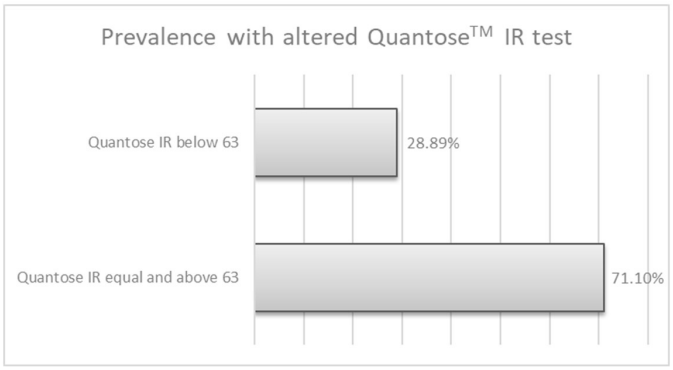

FIGURE 1. Prevalence of insulin resistance with Quantose ™ IR.

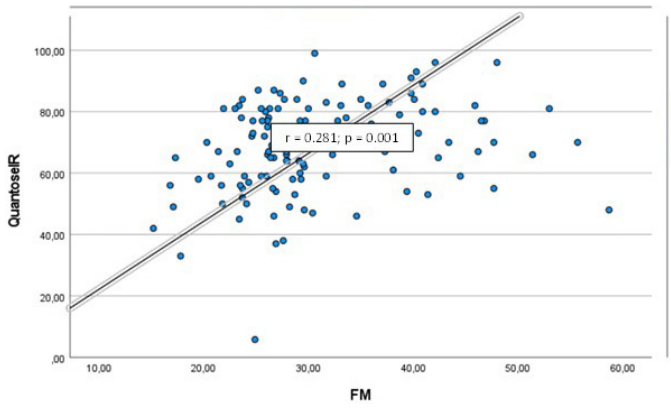

FIGURE 2. Correlation between Quantose™ IR and FM (%).

Pearson's correlation. FM: Fat mass.

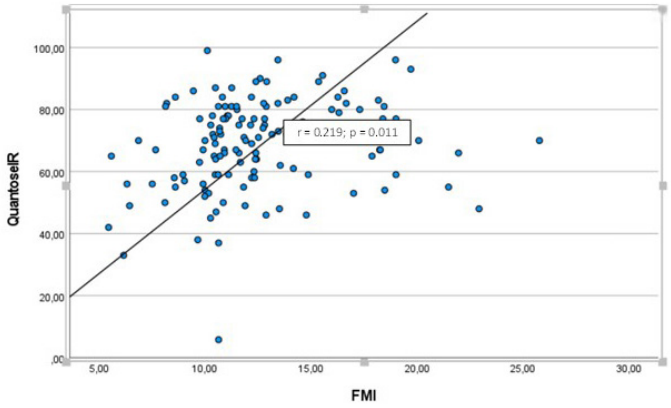

FIGURE 3. Correlation between Quantose™ IR and FMI.

Pearson's correlation. FMI: Fat mass index.

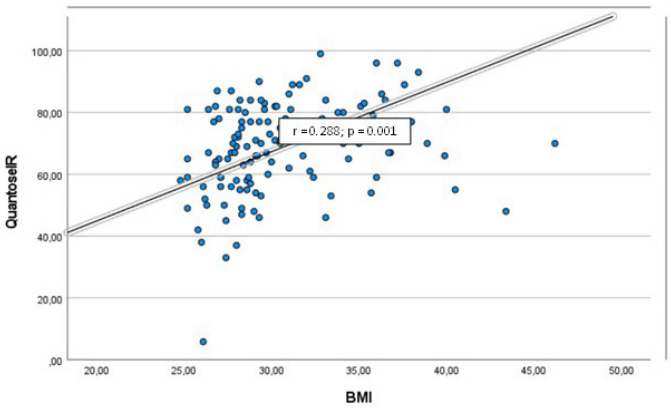

FIGURE 4. Correlation between Quantose™ IR and BMI.

Pearson's correlation. BMI: Body mass index.

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Table 2. Mean comparison between FM, FMI, and BMI and insulin resistance measured by Quantose™ IR.

	Altered Quantose™ IR				
	Present ≥ 63 (n = 94)		Absent < 63 (n = 41)		
	Mean	SD	Mean	*SD*	*p*
FM (%)	32.4	7.9	28.0	8.6	0.004
FMI (m/kg^2)	13.2	3.5	11.5	3.8	0.024
BMI (m/kg^2)	31.4	3.9	29.2	3.9	0.004

T-test for independent samples. FM: Fat mass. FMI: Fat mass index. BMI: Body mass index.

DISCUSSION

This study highlights the importance of the integral evaluation of patients with metabolomic and anthropometric measurements. Results show that Quantose™ IR positively correlates with FM, FMI, and BMI at a statistically significant level, indicating a physiopathological correlation. This evidence points at the importance of using tests as Quantose™ IR in patients with higher weight and body mass to identify their health status.

In our study, the prevalence of insulin resistance among patients with prediabetes was 71%, according to the Quantose™ IR test. In the pilot study by San Mauro et al. (2019) in a Spanish pediatric sample with risk factors for diabetes, the prevalence rate of insulin resistance measured with the Quantose™ IR test was 90.9%.[16] This is one of scarce studies worldwide that report the use of the Quantose™ IR test.

The prevalence of prediabetes in Mexico is 43%, while adult obesity rates are the second highest in the world.[3] It is necessary to implement medical nutritional strategies focused on modifying at-risk patients' lifestyle, following up with biomarkers as Quantose™ IR and BIA. Both of them can help establish strategies with pharmacological treatment. The results of this study identify a group of high-risk patients that can benefit from an early treatment strategy.

In our study, it was more common to see Quantose™ IR alterations among patients with a higher accumulation of FM and weight. Similarly, Cobb et al. (2013) showed that most patients with prediabetes are of a higher age group, overweight, and obese.[5] Cobb et al. suggest that traditional diagnostic tests do not measure insulin resistance directly, limiting the precision of an early diagnosis.[5] Tripathy et al. conclude that the Quantose™ IR test is a tool that may benefit patients due to its sensitivity in the early stages of the disease.[17]

It is important to contribute to the evidence through studies with larger sample sizes in populations with clinical characteristics similar to ours. This will enable the comparison of results to provide recommendations in clinical practice guides that prioritize tests such as Quantose™ IR and BIA anthropometric measurement indicators.

In addition, patients with prediabetes diagnosis and an altered Quantose™ IR test, who receive intensive pharmacological and non-pharmacological intervention, may have the possibility of remission.[18]

CONCLUSIONS

We can conclude that there is a positive and statistically significant correlation between the metabolomic biomarker Quantose™ IR and anthropometric measurements, such as fat mass, fat mass index evaluated through electrical bioimpedance, and body mass index in prediabetic patients. This is useful for everyday practice in the diagnosis and management of patients with prediabetes, overweight, and obesity.

CONFLICT OF INTEREST

The authors declare there are no conflicts of interest. This study was funded by the *Clínicas de Salud Incluyente y Educación* [Education and Inclusive Health Clinics] at *Centro Médico ABC* [ABC Medical Center].

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Appendix A. Measurement units.

FM %

FMI kg/m^2

BMI kg/m^2

Appendix B. Abbreviations.

Electrical bioimpedance analysis: BIA

Fat mass: FM

Fat mass index: FMI

Homeostatic model assessment of insulin resistance: HOMA

Hydroxybutyric Acid: α-HB

Linoleoylglycerophosphocholine: L-GPC

College of American Pathologists: CAP

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