Journal of Diabetes & Metabolism
ISSN: 2155-6156

Bermúdez et al., J Diabetes Metab 2016, 7:6
DOI: 10.4172/2155-6156.1000683

Research Article Open Access

Prevalence and Risk Factors associated with Impaired Fasting Glucose in Adults from Maracaibo City, Venezuela

Valmore Bermúdez[1]*, Juan Salazar[1], Robys González[1], Angel Ortega[1], María Calvo[1], Luis Carlos Olivar[1], Jessenia Morillo[1], Edgar Miquilena[1], Mervin Chávez-Castillo[1], Rendy Chaparro[1], Mayela Cabrera[1] and Joselyn Rojas[1,2]

[1]*Endocrine and Metabolic Diseases Research Center, University of Zulia, Maracaibo, Venezuela*
[2]*Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA. 02115, USA*

Abstract

Objective: The purpose of this study was to evaluate the prevalence and risk factors associated with impaired fasting glucose (IFG) in adult individuals from Maracaibo city, Venezuela.

Materials and methods: 2230 patients from the Maracaibo Metabolic Syndrome Prevalence Study were selected. IFG was defined according to the 2016 ADA criteria. A multiple logistic regression model was constructed in order to assess risk factors associated with IFG.

Results: In the general population, the prevalence of IFG was 19.5% (n=435), with 46.4% (n=202) being women and 53.6% (n=233) being men, p=0.004. The main risk factors associated with IFG were age (≥60 years: OR=2.31; CI 95%=1.23-4.35; p<0.01), alcohol consumption, abdominal obesity and insulin resistance. After evaluating individuals with IFG exclusively, the major risk factor was the presence of elevated high-sensitivity C-Reactive Protein levels (OR=2.03; CI 95%=1.13-3.67; p<0.02).

Conclusions: In Maracaibo the prevalence of IFG is similar to that of international reports. It is associated with a variety of risk factors, especially abdominal obesity, insulin resistance and low-grade inflammation, demonstrating the close link between adiposopathy and alterations in glucose metabolism.

Keywords: Impaired fasting glucose; Insulin resistance; Obesity; Physical activity; Hypertension; Inflammation; Diabetes

Introduction

Type 2 Diabetes Mellitus (T2D) is responsible for approximately 4.9 deaths a year worldwide, with a projected 59% increase in these estimates by year 2035 [1]. In 2003, the American Diabetes Association (ADA) recognized an intermediate metabolic stage in which blood glucose levels are higher than normal range but do not reach the diagnostic criteria for T2D, leading to the birth of the concepts of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) [2]; often grouped together and termed "Pre-Diabetes" [3]. Recently, the prevalence of this metabolic alteration in American adults was found to be 37% in the general population, and 51% in subjects older than 65 years of age [4]. In subjects classified as pre-diabetics, IFG appears to be twice as frequent as IGT [5], representing an important risk factor for T2D [6].

The pathophysiology of IFG has been described to involve hepatic insulin resistance and a deficient early phase insulin secretion [7]. Therefore, IFG is often associated with overweight and obesity, both common in populations with deleterious habits and risk factors such as physical inactivity, high-calorie diets, excessive alcohol consumption and smoking [8]; all of which contribute to progressive dysfunction of pancreatic beta cells, a mechanism shared with T2D, but present in a less severe form in IFG [9].

Identification of patients with IFG is clinically relevant, considering that changes in lifestyle and potential pharmacological intervention could reduce the risk of advancing into T2D and favor regression to euglycemia [10,11]. In view of the scarcity of reports on the epidemiological behavior of this metabolic disorder in our locality, the purpose of this study was to evaluate the prevalence and risk factors associated with impaired fasting glucose (IFG) in adult individuals from the Maracaibo city, Venezuela.

Materials and Methods

Subjects selection

The sample method has been already published in the Maracaibo City Metabolic Syndrome Prevalence Study cross-sectional proposal [12], yet the main aspects will be mentioned. This was a cross-sectional, descriptive, randomized, multistage study which enrolled a total of 2,230 subjects. The study was approved by the Bioethics Committee of the Endocrine and Metabolic Diseases Research Center – University of Zulia, and all participants signed a written consent before being interrogated and physically examined by a trained team.

Subjects evaluation

Data were collected through completion of a full clinical record carried out by trained personnel, who encompassed interrogation on personal and family history of endocrine and cardiovascular disease, and determination of socioeconomic status by the Graffar scale modified by Méndez-Castellano [13].

Based on information obtained during the clinical interview, subjects were categorized by their smoking habits as follows [14]: a)

***Corresponding author:** Valmore Bermúdez, University of Zulia, Endocrine and Metabolic Diseases Research Center "Dr. Félix Gómez" Av. 20, Maracaibo 4004, Venezuela, Tel: +582617597279; E-mail: valmore@gmail.com

Received April 25, 2016; **Accepted** June 29, 2016; **Published** June 30, 2016

Citation: Bermúdez V, Salazar J, González R, Ortega A, Calvo M, et al. (2016) Prevalence and Risk Factors associated with Impaired Fasting Glucose in Adults from Maracaibo City, Venezuela. J Diabetes Metab 7: 683. doi:10.4172/2155-6156.1000683

Non-Smokers, individuals who had never smoked, or had smoked <100 cigarettes in their lifetime; b) Current Smokers, subjects who had smoked ≥100 cigarettes in their lifetime, or reported current habitual smoking at the time of evaluation, or had quit smoking less than one year prior to our assessment; and c) Past Smokers, individuals who had consumed ≥100 cigarettes in their lifetime and quit over one year prior to our questioning. Regarding alcohol intake, drinkers were defined as subjects who consumed ≥1 gram of alcohol daily [15].

Physical activity (PA) was assessed with the International Physical Activity Questionnaire (IPAQ) [16]. For statistical analysis, PA was evaluated in 4 domains: Occupational, Household, Transport and Leisure. In each of these domains, subjects were categorized as: a) Inactive, MET/week=0; or b) Active, MET/week>0. The latter were then subcategorized by gender-specific MET/week quintiles in each domain.

Clinical evaluation

Blood pressure (BP) was taken with subjects sitting down with their feet on the floor following 15 minutes of rest, determined through the auscultatory method with a calibrated mercury sphygmomanometer; identifying Korotkoff's phases I and V as systolic and diastolic BP respectively. BP was determined 3 times, with 15 minutes in between each take, on two different days; results were classified by the Eighth Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) guidelines [17].

An electrical bioelectric scale was used to obtain weight (Tanita, TBF-310 GS Body Composition Analyzer, Tokyo – Japan). Height was measured using a calibrated metric measurement tape, with the subject standing up barefoot. Body Mass Index (BMI) was calculated with the formula: [weight/height2] expressing results as kg/m^2. According to their BMI, subjects were sorted in 3 categories: a) BMI ≤ 24.9; b) 25-29.9; and c) ≥30 [18]. Waist circumference (WC) was evaluated with calibrated measuring tapes in accordance to the anatomical landmarks proposed by the USA National Institutes of Health protocol [19].

Laboratory analysis

Overnight fasting determination of glucose, total cholesterol, triacylglycerides (TAG), and HDL-C was done with an automated analyzer (Human Gesellschaft für Biochemica und Diagnostica mbH, Germany); the intra-assay variation coefficients for total cholesterol, TAG, and HDL-C were 3%, 5%, and 5%, respectively. LDL-C and VLDL-C levels were calculated applying Friedewald's formula [20] but when TAG levels were <400 mg/dL. LDL-C concentrations were directly measured through lipoprotein electrophoresis and densitometry with a BioRad GS-800 optical densitometer. Insulin was quantified using ultrasensitive ELISA double-sandwich methodology (DRG Instruments GmbH, Germany, Inc.). Serum high-sensitivity C-Reactive Protein (hs-CRP) was quantified through immunoturbidimetric assays (Human Gesellschaft fur¨Biochemica und Diagnostica mbH, Germany).

Definitions

Subjects having the following characteristics were operatively classified as having T2D: a) Those with a previously established diagnosis of T2D; and b) Those without personal history of T2D but with fasting glucose ≥ 126 mg/dL (2). On the other hand, non-diabetic subjects were classified as follows: a) normoglycemic (NG), individuals with fasting glucose<100 mg/dL; and b) Impaired Fasting Glucose (IFG) those fasting glycemia 100-126 mg/dL [21].

As per the IDF/NHLBI/AHA/WHF/IAS/IASO-2009 consensus criteria [22], abdominal obesity was defined as waist circumference≥80 cm in females or ≥90 cm in males. Likewise, we use local waist circumference cutoff points ≥ 90 cm (females) and ≥95 cm (males) in abdominal obesity definition [23].

Regarding a lipid definition, hypertriacylglyceridemia was defined as fasting TAG ≥150 mg/dL; and low HDL-C as fasting HDL-C<50 mg/dL in females or <40 mg/dL in males. HOMA2-IR was utilized for the evaluation of insulin resistance (IR) as proposed by Levy et al. computed with the HOMA-Calculator v2.2.2 software application, IR was defined as HOMA2-IR ≥ 2 [24] and elevated hs-CRP was defined as levels ≥ 0.765 mg/L [25].

Statistical Analysis

Qualitative variables were expressed as absolute and relative frequencies, evaluating association through Pearson's Chi-squared (χ^2) test. Quantitative variables were evaluated for distribution normality with Geary's test and were expressed as arithmetic means ± SD. Variables with non-normal distribution underwent logarithmic transformation; when normalization could not be achieved (TAG, HDL-C hs-CRP), these variables were expressed as medians (25th percentile-75th percentile). One-Way ANOVA or Kruskal-Wallis tests were applied to evaluate differences between means or medians, respectively.

A multiple logistic regression model was constructed in order to estimate odds ratios (Confidence Interval 95%) for the presence of IFG, adjusted by gender, age groups, ethnic groups, socioeconomic status, educational status, marital status, occupational status, smoking habits, leisure-domain PA, presence of high TAG, presence of low HDL-C, JNC-8 classification, presence of elevated WC, BMI classification, presence of elevated hs-CRP and presence of IR. A second model was constructed, introducing adjustment for presence of elevated hs-CRP, and local abdominal obesity definition to waist circumference (Females: ≥90 cm; Males: ≥95 cm).

In addition, an ordinal logistic regression model was constructed, with fasting glucose tertiles among subjects with IFG set as the dependent variable. The independent variables included gender, age groups, ethnic groups, abdominal obesity, hypertriglyceridemia, low HDL-C, BMI classification, JNC-8 classification, TAG/HDL-C ratio tertiles, elevated hs-CRP and presence of IR. Regression coefficients (β) were calculated with their corresponding confidence intervals (95% CI) along with Odds Ratios (e^{β}) and their 95% CI. Goodness-of-fit parameters were calculated and parallel line testing was performed. Data were analyzed with the Statistical Package for the Social Sciences (SPSS) v.21 for Windows (IBM Inc. Chicago, IL), and de results were considered statistically significant when $p<0.05$.

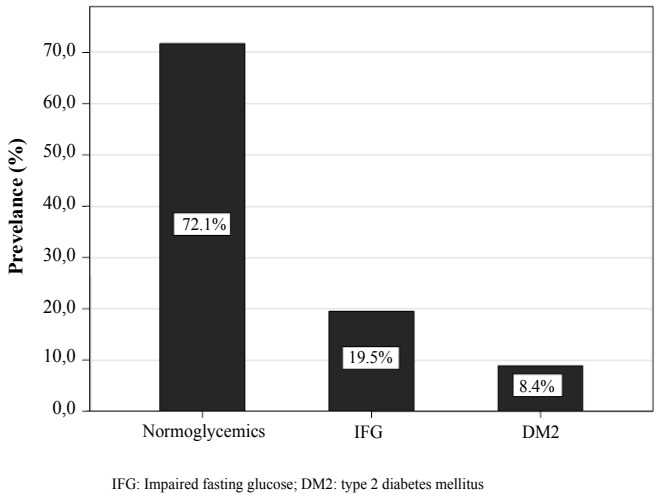
Results

Characteristics of the general population

The sample had 2,230 individuals, 52.6% were women (n=1172) with a mean age of 39.3 ± 15.4. The prevalence of DM2 was 8.4% (n=187) and the prevalence of IFG was 19.5% (n=435) (Figure 1).

Sociodemographic and psycobiological characteristics according to IFG

Table 1 shows the prevalence of IFG according to sociodemographic and psychobiological habits of the population. Age groups showed the greatest degree of association, displaying a rising prevalence of IFG, from 12.1% (n=91) in individuals aged <30 and years, to 31% in those



IFG: Impaired fasting glucose; DM2: type 2 diabetes mellitus

Figure 1: Prevalence of type 2 diabetes mellitus and impaired fasting glucose. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

aged ≥ 60 years (n=54, χ^2=63.47; p<0.001). In contrast, regarding leisure-time PA, prevalence of IFG was highest in subjects classified as inactive (22.1%; n=270), and lowest in subjects in Q5 (11%; n=20), χ^2=15.80; p=0.007.

Clinical characteristics according to IFG

Among all clinical features studied (Table 2), IR appeared to be the most closely related to IFG, with these disorders coexisting in 31.4% of subjects (n=252) (χ^2=75.44; p<0.0001). BP classification by the JNC-8 was also tightly linked to IFG, with a 15.7% prevalence in normotensive subjects vs 32.9% in hypertensives; χ^2=50.01; p<0.0001.

Risk factors for IFG

Evaluation of the correlation between risk factors in a multivariate context revealed the presence of IR to be the most important risk factor for IFG in our population (OR=2.51; 95%CI=1.79-3.52; p<0.01), followed by age groups (≥60 years: OR=2.31; 95%CI=1.23-4.35; p<0.01) (Table 3).

Clinical and biochemical characteristics of subjects with IFG

After assessing the behavior of various clinical and biochemical variables according to fasting glucose tertiles among subjects with IFG, a progressive worsening across tertiles was observed in most variables (Table 4). Although many variables showed a significant association with these fasting glucose tertiles, the presence of elevated hs-CRP was the main risk factor identified in the multivariate analysis (OR=2.03; 95%CI=1.13 to 3.67; p<0.02).

Discussion

IFG is an intermediate disglycemic stage that precedes T2D [5], which has displayed an alarming rise in prevalence in recent years [26,27]. Because of the possible disease-modifying potential of early therapeutic intervention in these subjects, it is of vital importance to evaluate the epidemiological behavior of this metabolic alteration and determine the main risk factors associated with it in our population.

In Latin America, the *CARMELA* study reported a prevalence of IFG of only 2%, with Mexico and Bogota boasting the highest figures. Meanwhile, the city of Barquisimeto in Venezuela reported only 1%

		Normoglycemics		Impaired Fasting Glucose		χ^2 (*p*)
		n	%	n	%	
Gender	Females	870	81.2	202	18.8	8.21 (0.004)
	Males	736	76.0	233	24.0	
Age groups (years)	<30	664	87.9	91	12.1	63.47 (<0.001)
	30-59	822	73.9	290	26.1	
	≥60	120	69.0	54	31.0	
Ethnic groups	Mixed race	1224	78.7	332	21.3	6.09 (0.19)
	Hispanic White	248	77.3	73	22.7	
	Afro-Venezuelan	42	72.4	16	27.6	
	Amerindian	81	86.2	13	13.8	
	Others	11	91.7	1	8.3	
Socioeconomic status	Classes I y II	319	75.8	102	24.2	4.71 (0.09)
	Class III	660	80.9	156	19.1	
	classes IV y V	627	78.0	177	22.0	
Occupational Status	Un- Employed	799	76.3	248	23.7	3.12 (0.08)
	Employed	668	79.7	170	20.3	
Family history	No	859	79.2	226	20.8	3.95 (0.27)
	T2D	702	78.5	192	21.5	
	Type 1 Diabetes Mellitus	25	80.6	6	19.4	
	Both of them	20	64.5	11	35.5	
Smoking Habits	Non-Smokers	1143	79.6	293	20.4	2.82 (0.24)
	Current Smokers	226	75.6	73	24.4	
	Past Smokers	230	77.2	68	22.8	
Alcohol Consumption	No	1139	80.9	269	19.1	13.19 (<0.001)
	Yes	467	73.8	166	26.2	
Physical activity (Work)	Inactive	1187	78.3	329	21.7	1.90 (0.86)
	Q1	83	79.8	21	20.2	
	Q2	82	76.6	25	23.4	
	Q3	83	79.8	21	20.2	
	Q4	89	83.2	18	16.8	
	Q5	82	79.6	21	20.4	
Physical activity (Transportation)	Inactive	569	78.6	155	21.4	3.92 (0.56)
	Q1	203	81.5	46	18.5	
	Q2	206	76.6	63	23.4	
	Q3	210	81.4	48	18.6	
	Q4	214	78.1	60	21.9	
	Q5	180	76.3	56	23.7	
Physical activity (Household)	Inactive	402	75.0	134	25.0	11.78 (0.04)
	Q1	236	81.1	55	18.9	
	Q2	252	81.8	56	18.2	
	Q3	257	82.1	56	17.9	
	Q4	220	75.1	73	24.9	
	Q5	239	79.7	61	20.3	
Physical activity (Leisure)	Inactive	949	77.9	270	22.1	15.80 (0.007)
	Q1	113	72.4	43	27.6	
	Q2	127	77.9	36	22.1	
	Q3	130	78,8	35	21,2	
	Q4	126	80,3	31	19.7	
	Q5	161	89.0	20	11.0	
Total§		**1606**	**78.7**	**435**	**21.3**	

§Subjects with T2D were excluded from the analysis

Table 1: Sociodemographic and psychobiological characteristics associated with the diagnosis of Impaired Fasting Glucose. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

	Normoglycemics		Impaired Fasting Glucose.		χ^2 (*p*)
	n	%	n	%	
Waist circumference[†]					30.53 (<0.0001)
Normal	470	87.0	70	13.0	
Elevated	1136	75.7	365	24.3	
Waist circumference[‡]					48.49 (<0.0001)
Normal	856	85.1	150	14.9	
Elevated	750	72.5	285	27.5	
Triacylglycerides (mg/dL)					47.25 (<0.0001)
<150	1256	82.3	270	17.7	
≥150	350	68.0	165	32.0	
HDL-C					3.43 (0.06)
Normal	711	80.6	171	19.4	
Lower	895	77.2	264	22.8	
BMI					28.78 (<0.001)
Normal weight	566	84.2	106	15.8	
Overweight	579	79.3	151	20.7	
Obesity	461	72.1	178	27.9	
JNC-8 Classification					50.01 (<0.0001)
Normotension	708	84.3	132	15.7	
Prehypertension	613	79.0	163	21.0	
Hypertension	285	67.1	140	32.9	
hs-CRP (mg/L)					4.86 (0.03)
<0.765	817	83.0	167	17.0	
≥0.765	237	77.5	69	22.5	
Insulin Resistance[¶]					75.44 (<0.0001)
Absent	892	85.4	152	14.6	
Present	550	68.6	252	31.4	
Total[§]	**1606**	**78.7**	**435**	**21.3**	

BMI=Body Mass Index; hs- CRP= High-sensitivity C-reactive protein; JNC-8=Eighth Joint National Committee
[†]Criteria by IDF Men: ≥90 cm; Women: ≥80 cm.
[‡]Criteria according local criteria (Men: ≥95 cm; Women: ≥90 cm).
[¶]HOMA2-IR ≥ 2
[§]They are excluded from the analysis of subjects with diabetes mellitus

Table 2: Clinical features associated with Impaired Fasting Glucose. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

	Model 1*				Modelo 2**	
	Crude Odds Ratio (CI 95%[a])	*p*[b]	Adjusted Odds Ratio (CI 95%[a])	*p*[b]	Adjusted Odds Ratio (CI 95%[a])	*p*[b]
Age groups (years)						
<30	1.00	-	1.00	-	1.00	-
30-49	2.57 (1.99 - 3.33)	<0.01	1.99 (1.46 - 2.71)	<0.01	2.09 (1.39 - 3.14)	<0.01
≥60	3.28 (2.23 - 4.84)	<0.01	2.47 (1.54 - 3.96)	<0.01	2.31 (1.23 - 4.35)	<0.01
Alcohol consumption[c]						
No	1.00	-	1.00	-	1.00	-
Yes	1.51 (1.21 - 1.88)	<0.01	1.28 (0.98 - 1.67)	0.07	1.49 (1.04 - 2.12)	0.03
Hypertriglyceridemia[f]						
Absent	1.00	-	1.00	-	1.00	-
Present	2.19 (1.75 - 2.75)	<0.01	1.42 (1.09 - 1.86)	0.01	1.35 (0.95 - 1.94)	0.09
JNC-8 Classification						
Normotense	1.00	-	1.00	-	1.00	-
Pre-hypertensive	1.43 (1.11 - 1.84)	<0.01	1.05 (0.78 - 1.40)	0.77	0.93 (0.54 - 1.35)	0.68
Hypertensive	2.64 (2.00 - 3.47)	<0.01	1.61 (1.15 - 2.25)	<0.01	1.19 (0.77 - 1.85)	0.44
Elevated Waist circumference						
Absent	-	-	1.00	-	1.00	-
Present	-	-	1.13 (0.79 - 1.59)	0.51	1.62 (1.07 - 2.45)	0.02
Insulin-resistance[g]						
Absent	1.00	-	1.00	-	1.00	-
Present	2.69 (2.14 - 3.38)	<0.01	2.33 (1.81 - 2.99)	<0.01	2.51 (1.79 - 3.52)	<0.01

a Confidence interval (95%); **b** Significance level; **c** Alcohol consumption > 1 gr/daily; **d** Triglycerides ≥ 150 mg/dL; **e** HOMA2-IR ≥ 2
***Model 1**: Adjustment for gender, age groups, ethnic groups, family history of diabetes mellitus, employment status, smoking habits, alcohol consumption, home-sphere physical activity, leisure-time physical activity, hypertriglyceridemia, low HDL -C, JNC-8 classification, BMI categories, presence of insulin resistance and elevated waist circumference: Men: ≥90 cm; Women: ≥80 cm.
****Model 2**: Similar adjustment to model 1 but elevated waist circumference is adjusted (Men: ≥95 cm; Women: ≥90 cm) and elevated hs-CRP (≥0,765 mg / L) is added.

Table 3: Logistic regression models of risk factors for Impaired Fasting Glucose. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

	Tertile 1 (100-102.9 mg/dL) [A]		Tertile 2 (103-107.9 mg/dL) [B]		Tertile 3 (≥ 108 mg/dL) [C]		*p**	A vs B	A vs C	B vs C
	Media	DE	Media	DE	Media	DE				
Age (years)	40.6	15.1	44.2	14.9	46.2	14.2	0.003	0.08	0.002	0.41
BMI (Kg/m²)	28.5	6.5	29.1	5.6	31.5	7.9	<0.001	0.75	0.001	0.006
Waist Circumference (cm)	95.6	15.1	97.7	13.3	104.0	18.8	<0.001	0.40	<0.001	0.004
Basal glycemia (mg/dL)	100.9	0.8	104.8	1.5	113.8	4.8	<0.001	<0.001	<0.001	<0.001
Insulin (UI/L)	15.8	8.6	18.2	14.3	18.7	10.9	0.100	0.60	0.09	0.43
HOMA2-βcell	133.2	48.2	134.9	65.5	120.2	46.9	0.03	0.91	0.05	0.09
HOMA2-S	53.1	26.9	53.1	47.9	45.3	25.1	0.03	0.51	0.02	0.22
HOMA2-IR	2.36	1.21	2.70	1.89	2.88	1.59	0.03	0.49	0.02	0.24
Total cholesterol (mg/dL)	193.4	42.0	203.9	60.1	208.1	47.7	0.03	0.24	0.02	0.52
Triacilglycerides (mg/dL)	132.8	96.7	143.8	112.8	167.2	109.5	<0.001	0.57	<0.001	0.008
HDL-C (mg/dL)	45.1	11.5	43.1	13.2	41.3	10.5	0.02	0.19	0.02	0.53
VLDL-C (mg/dL)	26.6	19.4	28.8	22.6	33.6	21.9	0.02	0.66	0.02	0.13
LDL-C (mg/dL)	122.8	36.2	130.9	44.2	134.5	39.9	0.09	0.51	0.07	0.51
Cholesterol Non HDL	148.2	41.5	160.8	60.2	166.8	48.0	0.009	0.11	0.007	0.56
Index TAG/HDL†	2.4	1.5-4.3	2.9	1.9-4.4	3.5	2.3-5.5	<0.001	-	-	-
Lipoprotein(a) (mg/dL)	28.6	12.9	26.9	15.9	25.4	14.5	0.209	0.62	0.18	0.65
Systolic blood pressure (mmHg)	120.9	17.9	122.8	17.6	125.7	16.7	0.04	0.59	0.03	0.24
Diastolic blood pressure (mmHg)	78.8	12.5	79.7	11.9	80.6	11.8	0.40	0.75	0.37	0.79
hs-CRP (mg/L)†	0.397	0.208-0.758	0.383	0.139-0.674	0.607	0.231-1.027	0.05	-	-	-

BMI= Body mass index; hs-CRP= high-sensitivity C-reactive protein.
*One-Way ANOVA (after logarithmic transformation) Post-hoc Tukey test.
†Expressed in median (p25-p75). Kruskall-Wallis Test comparison.

Table 4: Clinical and biochemical characteristics in subjects with Impaired Fasting Glucose according to fasting glucose tertiles. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

[28] of IFG prevalence. All of these are lower than estimations in the USA (26%) [4]. In contrast to the *CARMELA* study, the PERUDIAB study recently evaluated 1,677 Peruvian individuals aged ≥ 25 years, estimating a general IFG prevalence of 22.4% [29]. Reports on pre-diabetes are scarce in Venezuela, although there is a report from a rural population in Merida State, in the Andean Region, which found 18.6% of the individuals to have IFG [30], a similar rate to the findings in our study (19.5%).

Evaluation of IFG by gender showed a higher prevalence in males as has been described in other populations [31,32], similarly echoing previous reports [27,28,33], prevalence increasing with age in both univariate and multivariate analysis (Table 5). This might be associated with senescent changes, such as increased visceral adiposity [34] decreased lean mass [35] and reduced PA [36] all having a direct influence on IR development. The decrease in PA may play a particularly important role in this process, as PA improves glucose metabolism by favoring its uptake by target organs, depleting muscular glycogen, and inducing favorable changes in lipid metabolism [37,38].

Furthermore, alcohol consumption was associated with a higher risk of having this metabolic alteration, similar to findings reported by Cullmann et al. [39] in 111 pre-diabetic Swedish individuals, where alcohol consumption was recognized as a risk factor in men, mainly in beer drinkers (OR: 1.84, 95% CI: 1.13-3.01, p<0,05). This effect appears to be dependent on the amount and type of alcohol consumed, as for women, for example, the moderate consumption of wine was found to be protective, while the excessive consumption of spirituous beverages was identified as a risk factor (OR: 2.41, 95% CI 1.47-3.96). Additionally, our research group has demonstrated that the effect of alcohol consumption on the components of the metabolic syndrome appears to be dose-dependent in our population, with an approximate intake of 4-6 beers, 3-5 spirituous beverages or 4-7 cups of wine found to be a risk factor for hyperglycemia among males (OR: 1.99, 95%CI: 1.20-3.33; p<0.01) [40].

Regarding clinical characteristics, in the multivariate context the results showed that only subjects with abdominal obesity had a higher risk of IFG similar to results by Diaz et al. [8] in the PREDAPS study, where 1184 Spanish pre-diabetic individuals were evaluated. In this study, abdominal obesity was considered a risk factor in both genres, indeed obesity is closely related to metabolic disorders of carbohydrates, especially visceral adiposity. In the context of adiposopathy –characterized by increased signaling of pro-inflammatory cytokines such as TNF-α, MCP-1, IL-1β and macrophage infiltration in adipose tissue-[41] TNF-α interrupts the insulin signaling cascade by phosphorylating serine-threonine sidechains in the insulin receptor substrate (IRS) altering its enzymatic activity and preventing GLUT4 translocation in insulin-dependent tissues, being a molecular mechanism of utmost importance in IFG appearance [42]. In addition, TNF-α increases lipolysis and decreases biosynthesis of triacylglycerols via peroxisome proliferator-activated receptor gamma (PPARγ) signaling in adipose tissue, consequently causing an increase in free fatty acids (FFA) release into splanchnic circulation (43). According to Shulman et al. [43] this phenomenon favors FFA storage in ectopic tissues such as the liver and muscle, increasing the intracellular concentration of intermediates of fatty acid metabolism such as acyl-CoA, ceramides and diacylglycerol which are also involved in the phosphorylation of IRS and therefore in inhibiting effects [44], suggesting a close relationship between obesity, the presence of IR and the appearance of IFG.

Hypertension was also found to be a risk factor for IFG in our population, in resemblance to the PREDAPS study, where hypertensive subjects had a risk 2.33 times higher risk of IFG [8]. Nevertheless, this

	Tertile 1 (100-102.9 mg/dL)		Tertile 2 (103-107.9 mg/dL)		Tertile 3 (≥ 108 mg/dL)		χ^2 (*p*)	β* (CI95%); *p*	OR (CI95%)
	n	%	n	%	n	%			
Waist circumference‡							11.26 (0.004)		
Normal	55	36.7	53	35.3	42	28.0		0	
Elevated	68	23.9	96	33.7	121	42.5		0.12 (-0.88 – 0.65); 0.76	1.13 (0.41 – 1.91)
Triacilglycerides (mg/dL)							9.04 (0.01)		
<150	86	31.9	97	35.9	87	32.2		0	0
≥150	37	22.4	52	31.5	76	46.1		0.18 (-1.09 – 0.73); 0.69	1.19 (0.33 – 2.07)
HDL-C							4.42 (0.11)		
Normal	58	33.9	54	31.6	59	34.5		0	0
Low	65	24.6	95	36.0	104	39.4		-0.13 (-0.48 – 0.74); 0.67	0.87 (0.61 – 2.09)
BMI Classification							11.56 (0.02)		
Normal weight	37	34.9	39	36.8	30	28.3		0	0
Overweight	47	31.1	53	35.1	51	33.8		-0.15 (-0.95 – 0.62); 0.63	0.86 (0.39 – 1.86)
Obesity	39	21.9	57	32.0	82	46.1		0.63 (-0.82 – 0.95); 0.86	1.88 (0.44 – 2.59)
JNC-8 Classification							6.46 (0.17)		
Normotense	43	32.6	47	35.6	42	31.8		0	0
Pre-hypertensive	49	30.1	56	34.4	58	35.6		0.03 (-0.57 – 0.61); 0.96	1.03 (0.56 – 1.84)
Hypertensive	31	22.1	46	32.9	63	45.0		0.50 (-0.22 – 1.17); 0.17	1.64 (0.80 – 3.22)
hs-CRP (mg/L)							12.02 (0.002)		
<0.765	54	32.3	65	38.9	48	28.7		0	0
≥0.765	17	24.6	16	23.2	36	52.2		**0.71 (0.12 – 1.30); 0.02**	**2.03 (1.13 – 3.67)**
Insulinresistence¶							2.09 (0.35)		
Absent	44	28.9	58	38.2	50	32.9		0	0
Present	66	26.2	85	33.7	101	40.1		0.39 (-0.19 – 0.96); 0.17	1.48 (0.82 – 2.61)
TAG/HDL ratio							16.59 (<0.01)		
<1.74	39	31.7	34	22.8	22	13.5		0	
1.74-3.36	39	31.7	55	36.9	54	33.1		0.28 (-1.23 – 1.12); 0.93	1.32 (0.29 – 3.07)
>3.36	45	36.6	60	40.3	87	53.4		-0.05 (-0.49 – 1.04); 0.48	0.95 (0.61 – 2.83)
Total§	**123**	**28.3**	**149**	**34.3**	**163**	**37.4**			

BMI = body mass index; JNC-8 = 8th National Joint Committee for Hypertension
‡Criteria according to EPSMM (Men: ≥95 cm; Women: ≥90 cm).
¶HOMA2-IR ≥ 2
§Subjects with diabetes mellitus were excluded from the analysis
*Ordinal regression model adjusted for gender, age groups, ethnic groups, leisure time physical activity, abdominal obesity, hypertriglyceridemia, low HDL-C, BMI classification, JNC-8 classification, elevated hs-CRP and presence of insulin resistance.
Model adjustment information: (χ^2 = 34.69; p = 0.007)
Pseudo R-Squared: Cox and Snell (0.14) - Nagelkerke (0.16) - McFadden (0.07)
Parallel line test (χ^2 = 14.17; p = 0.66)

Table 5: Clinical characteristics in patients with Impaired Fasting Glucose according to fasting glucose tertiles. Maracaibo City Metabolic Syndrome Prevalence Study, 2016.

association was no longer significant after adjusting the model by abdominal circumference and elevated hs-CRP, which might imply that this co-relation between hypertension and alteration of IFG depends on other factors different from IR, such as a certain level of chronic inflammation and oxidative stress, as has been proposed in previous publications [45].

Finally, when evaluating individuals with IFG exclusively, we observed that clinical and metabolic parameters are altered by increasing levels of glycemia. Moreover, when multivariate analysis revealed the presence of elevated hs-CRP to be the factor to most closely related to the highest tertile of fasting glycemia, similar to the findings of Jaiswal et al. [46]. Indeed, prospective studies have described elevated hs-CRP as an independent risk factor for the development of both T2D [47] and pre-diabetes [48], being considered as a chronic inflammation marker closely related to IR, and playing a central role in the development and progression of IFG, metabolic syndrome and T2D [49]. It is also important to note that elevated hs-CRP was a significant risk factor only when analyzing subjects with IFG. Molecular mechanisms that could explain this unique correlation in this group of subjects may be an upregulation of CRP expression by IR state, counteracting the physiological effects of insulin in early phase synthesis of hepatic proteins [50], existing major acute phase protein synthesis, which might explain why hs-CRP is a better predicting factor only in patients with established metabolic disorders.

Limitations of this study include its cross-sectional design, which does not allow establishment of causality, and the lack of assessment of nutritional habits, which repr sent an important factor contributing to dysglycemia. Likewise, even though there are many markers for low grade inflammation, hs-CRP was the only one who rendered significant results in the multivariant analysis. However, more research is required in order to properly depict the mechanistics of this association in our population. Finally, the design of the study did not originally include the evaluation of 2 hr oral glucose tolerance test or postpandrial measurements. Nevertheless, in the upcoming second phase of the project, we are considering this variable as a new inclusion in our research.

In conclusion, our results highlight the responsibility of clinicians for the early detection of subjects with IFG, especially in populations with high prevalence of risk factors such as obesity, physical inactivity and metabolic syndrome [51-53]. IFG prevalence in our population is similar to worldwide reports, in contrast to the low prevalence previously reported in Latin America in past decades. IFG is also linked to various cardiovascular risk factors in our population such as age, alcohol consumption, abdominal obesity; suggesting these patients as candidates for early therapeutic intervention as recommended by the ADA [54]. Lastly, hs-CRP may be a useful predicting factor for T2D among subjects with IFG.

Funding

This work was supported by research grant Nº CC-0437-10-21-09-10 from the Technological, Humanistic, and Scientific Development Council (Consejo de Desarrollo Científico, Humanístico y Tecnológico; CONDES), University of Zulia, and research grant Nº. FZ-0058-2007 from Fundacite-Zulia.

Disclosure

The authors have are no conflicts of interest to disclose.

References

1. International Diabetes Federation (2013) International Diabetes Atlas [online version] 6th edn Brussels, Belgium: International Diabetes Federation 12: 6-9.
2. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, et al. (2003) Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 26: 3160-3167.
3. American Diabetes Association (2014) Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 37: S81-S90.
4. CDC (2011) National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States. Atlanta, GA: US Department of Health and Human Services 22: 13-27.
5. Cowie CC, Rust KF, Ford ES, Eberhardt MS, Byrd-Holt DD, et al. (2009) Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. Diabetes Care 32: 287-294.
6. Yeboah J, Bertoni AG, Herrington DM, Post WS, Burke GL (2011) Impaired fasting glucose and the risk of incident diabetes mellitus and cardiovascular events in an adult population: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 58: 140-146.
7. Abdul-Ghani MA, Tripathy D, DeFronzo RA (2006) Contributions of beta-cell dysfunction and insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting glucose. Diabetes Care 29: 1130-1139.
8. Díaz-Redondo A, Giráldez-García C, Carrillo L, Serrano R, García-Soidán FJ, et al. (2015) Modifiable risk factors associated with prediabetes in men and women: a cross-sectional analysis of the cohort study in primary health care on the evolution of patients with prediabetes (PREDAPS-Study). BMC Fam Pract 16: 5.
9. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, et al. (2007) Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care 30: 753-759.
10. Tuso P (2014) Prediabetes and lifestyle modification: time to prevent a preventable disease. Perm J 18: 88-93.
11. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, et al. (2006) Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet 368: 1096-1105.
12. Bermúdez V, Marcano RP, Cano C, Arráiz N, Amell A, et al. (2010) The Maracaibo city metabolic syndrome prevalence study: design and scope. Am J Ther 17: 288-294.
13. Méndez-Castellano H, De Méndez MC (1986) Estratificación social y biología humana: método de Graffar modificado. Arch Ven Pueric Pediatr 49: 93-104.
14. Zhang XF, Attia J, D'Este C, Yu XH (2004) Prevalence and magnitude of classical risk factors for stroke in a cohort of 5092 Chinese steelworkers over 13.5 years of follow-up. Stroke 35: 1052-1056.
15. Bermúdez V, Torres Y, Apruzzese V, Martínez MS, Chávez M, et al. (2014) Alcohol drinking patterns in the adult population from the Maracaibo municipality, Zulia – Venezuela. Revista Latinoamericana de Hipertensión 9: 21-28.
16. (2015) International Physical Activity Questionnaire.
17. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, et al. (2014) evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 311: 507-520.
18. World Health Organization (2003) The World Health Report 2: 32-41.
19. Holt JB, Huston SL, Heidari K, Schwartz R, Gollmar CW, et al. (2015) Indicators for chronic disease surveillance - United States, 2013. MMWR Recomm Rep 64: 1-246.
20. Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18: 499-502.
21. Chamberlain JJ, Rhinehart AS, Shaefer CF, Neuman A (2016) Diagnosis and Management of Diabetes: Synopsis of the 2016 American Diabetes Association Standards of Medical Care in Diabetes. Ann Intern Med 164: 542-52.
22. Alberti K, Eckel R, Grundy S, Zimmer PZ, Cleeman JI, et al. (2009) Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention: National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Circulation 120: 1640-1645.
23. Bermúdez V, Rojas J, Salazar J, Anez R, Chávez-Castillo M, et al. (2014) Optimal Waist Circumference Cut-Off Point for Multiple Risk Factor Aggregation: Results from the Maracaibo City Metabolic Syndrome Prevalence Study. Epidemiology Research International 718571.
24. Bermúdez V, Rojas J, Martínez MS, Apruzzese V, Chávez-Castillo M, et al. (2014) Epidemiologic Behavior and Estimation of an Optimal Cut-Off Point for Homeostasis Model Assessment-2 Insulin Resistance: A Report from a Venezuelan Population. International Scholarly Research Notices 6: 162-171.
25. Bermúdez V, Cabrera M, Mendoza L, Chávez M, Martínez MS, et al. (2013) Epidemiological behavior of high –sensitivity C-Reactive Protein (hs-CRP) in adult individuals in the Maracaibo city, Venezuela. Revista Latinoamericana de Hipertensión 8: 16-24.
26. Bullard KM, Saydah SH, Imperatore G, Cowie CC, Gregg EW, et al. (2013) Secular changes in U.S. Prediabetes prevalence defined by hemoglobin A1c and fasting plasma glucose: National Health and Nutrition Examination Surveys, 1999-2010. Diabetes Care 36: 2286-2293.
27. Sahai S, Vyas D, Sharma S (2011) Impaired Fasting Glucose: A Study of its Prevalence Documented at a Tertiary Care Centre of Central India and its Association with Anthropometric Variables. JIACM 12: 187-192.
28. Escobedo J, Buitrón LV, Velasco MF, Ramírez JC, Hernández R, et al. (2009) High prevalence of diabetes and impaired fasting glucose in urban Latin America: the CARMELA Study. Diabet Med 26: 864-871.
29. Seclen S, Rosas M, Arias A, Huayta E, Medina C (2015) Prevalence of diabetes and impaired fasting glucose in Peru: report from PERUDIAB, a national urban population-based longitudinal study. BMJ Open Diab Res Care 3: e000110.
30. González-Rivas JP, Nieto-Martínez R, Molina T, García RJ, Ugel E, et al. (2011) Prevalencia de síndrome metabólico, obesidad y alteración de la glucemia en ayunas en adultos del páramo del Estado Mérida, Venezuela (estudio VEMSOLS). Med Inter¬na (Caracas) 27: 262-267.
31. Hilawe EH, Yatsuya H, Kawaguchi L, Aoyama A (2013) Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucosetolerance in sub-Saharan Africa: a systematic review and meta-analysis. Bull World Health Organ 91: 671D-682D.
32. Williams JW, Zimmet PZ, Shaw JE, de Courten MP, Cameron AJ, et al. (2003) Gender differences in the prevalence of impaired fasting glycaemia and impaired glucose tolerance in Mauritius. Does sex matter? Diabet Med 20: 915-920.
33. Henry P, Thomas F, Benetos A, Guize L (2002) Impaired fasting glucose, blood pressure and cardiovascular disease mortality. Hypertension 40: 458-463.
34. Michalakis K, Goulis DG, Vazaiou A, Mintziori G, Polymeris A, et al. (2013) Obesity in the ageing man. Metabolism 62: 1341-1349.

35. Atkins JL, Whincup PH, Morris RW, Wannamethee SG (2014) Low muscle mass in older men: the role of lifestyle, diet and cardiovascular risk factors. J Nutr Health Aging 18: 26-33.

36. León-Latre M, Moreno-Franco B, Andrés-Esteban EM, Ledesma M, Laclaustra M, et al. (2014) Sedentary lifestyle and its relation to cardiovascular risk factors, insulin resistance and inflammatory profile. Rev Esp Cardiol (Engl Ed) 67: 449-455.

37. Borghouts LB, Keizer HA (2000) Exercise and insulin sensitivity: a review. Int J Sports Med 21: 1-12.

38. Gregg EW, Gerzoff RB, Caspersen CJ, Williamson DF, Narayan KM (2003) Relationship of walking to mortality among US adults with diabetes. Arch Intern Med 163: 1440-1447.

39. Cullmann M, Hilding A, Östenson CG (2012) Alcohol consumption and risk of pre-diabetes and type 2 diabetes development in a Swedish population. Diabet Med 29: 441-452.

40. Bermúdez V, Martínez MS, Chávez-Castillo M, Olivar LC, Morillo J, et al. (2015) Relationship between Alcohol Consumption and Components of the Metabolic Syndrome in Adult Population from Maracaibo City, Venezuela. Advances in Preventive Medicine 35: 25-47.

41. Xu H, Barnes GT, Yang Q, Tan G, Yang D, et al. (2003) Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. J Clin Invest 112: 1821-1830.

42. Bouzakri K, Zierath JR (2007) MAP4K4 gene silencing in human skeletal muscle prevents tumor necrosis factor-alpha-induced insulin resistance. J Biol Chem 282: 7783-7789.

43. Guilherme A, Virbasius JV, Puri V, Czech MP (2008) Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. Nat Rev Mol Cell Biol 9: 367-377.

44. Shulman GI (2000) Cellular mechanisms of insulin resistance. J Clin Invest 106: 171-176.

45. Ruiz-Nunez B, Pruimboom L, Dijck-Brouwer DA, Muskiet FA (2013) Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context. J Nutr Biochem 24: 1183-1201.

46. Jaiswal A, Tabassum R, Podder A, Ghosh S, Tandon N, et al. (2012) Elevated level of C-reactive protein is associated with risk of prediabetes in Indians. Atherosclerosis 222: 495-501.

47. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM (2001) C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 286: 327-334.

48. Doi Y, Kiyohara Y, Kubo M, Tanizaki Y, Okubo K, et al. (2005) Relationship between C-reactive protein and glucose levels in community-dwelling subjects without diabetes: the Hisayama Study. Diabetes Care 28: 1211-1213.

49. Pickup JC, Crook MA (1998) Is type II diabetes mellitus a disease of the innate immune system? Diabetologia 41: 1241-1248.

50. Campos SP, Baumann H (1992) Insulin is a prominent modulator of the cytokine-stimulated expression of acute-phase plasma protein genes. Moll Cell Biol 12: 1789-1797.

51. Bermúdez V, Pacheco M, Rojas J, Córdova E, Velázquez R, et al. (2012) Epidemiologic behavior of obesity in the Maracaibo City metabolic syndrome prevalence study. PLoS One 7: e35392.

52. Bermúdez VJ, Rojas JJ, Córdova EB, Añez R, Toledo A, et al. (2013) International physical activity questionnaire overestimation is ameliorated by individual analysis of the scores. Am J Ther 20: 448-458.

53. Bermúdez V, Rojas J, Salazar J, Calvo MJ, Morillo J, et al. (2014) The Maracaibo city metabolic syndrome prevalence study: primary results and agreement level of 3 diagnostic criteria. Revista Latinoamericana de Hipertensión 9: 20-31.

54. [No authors listed] (2016) Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care 39 Suppl 1: S4-5.