Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 722–729

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

# Hypertriglyceridaemic waist is associated with hyperuricaemia and metabolic syndrome in rheumatoid arthritis patients

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A R T I C L E   I N F O

*Article history:*
Received 13 November 2018
Accepted 29 November 2018

*Keywords:*
Hypertriglyceridaemic waist
Hyperuricaemia
Rheumatoid arthritis

A B S T R A C T

*Background:* /Aim: The hypertriglyceridaemic waist (HTGW) phenotype has been described and suggested in general population as a cardiovascular risk marker. The aim of the present study was to evaluate the HTGW phenotype as a marker related to HUC and MetS in rheumatoid arthritis (RA).
*Materials and methods:* This was a cross-sectional study was designed in 250 RA Mexicans patients. The HTGW phenotype was defined as elevated waist circumference and elevated triglyceride concentration. Logistic regression analysis was used to evaluate the association between the HTGW phenotype, HUC and MetS in its traditional NCEP/ATPIII versions and modified (HTGWm and MetSm).
*Results:* The prevalence of HTGW and HTGWm it was 20.4% and 32%, respectively. All patients with HTGW presented MetS ($P < 0.001$), and in a multivariate model, the HTGW phenotype was the marker most closely related to HUC in comparison to components of MetS.
*Conclusion:* The HTGW may represent a marker for screening of cardiometabolic risk in RA patients, so in clinical practice can be implemented as a low-cost marker in the evaluation of the patient regardless of clinical characteristics of disease.



## 1. Introduction

The hypertriglyceridaemic waist (HTGW) phenotype is defined as elevated waist circumference and serum triglyceride levels; HTGW has been described and suggested as a cardiovascular risk marker that allows cardiometabolic alterations to be identified [1,2]. The NCEP-ATPIII criteria allow the evaluation of cardiovascular risk (CVR) in a clinically healthy population [3] and have been suggested as the best criteria for the evaluation of HTGW. In patients with rheumatoid arthritis (RA), the chronic inflammatory process characteristic of the disease increases the CVR, so it is necessary to implement the use of new markers related to the increased co-morbidity in patients. The HTGW phenotype is newly associated with the presence of hyperuricaemia (HUC) [4]; high uric acid (UA) levels have been suggested as a metabolic and CVR marker as it relates to the process systemic inflammation and activation of the innate immune response involved in the pathogenesis of cardiovascular disease (CVD) [5], establishing the relationship between HUC and the pathogenesis of metabolic, haemodynamic and systemic disorders, which are frequent in RA [6]. The frequency of HUC in the general population is 12.1% [7], and up to 18.1% in patients with RA [8]. In a population without RA, HUC is related to the presence of low levels of high-density lipoprotein cholesterol (HDL-c), high blood pressure, hypertriglyceridaemia [9] and increased waist circumference [10]; it has been determined

*Abbreviations:* Anti-CCPs, anti-cyclic citrullinated peptide antibodies; BMI, body mass index; CVD, cardiovascular disease; CVR, cardiovascular risk; DAS28, disease activity score 28; DBP, diastolic blood pressure; DMARDs, disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; EWNT/NWET, enlarged waist-normal triglycerides/normal waist-elevated triglycerides; EWNT/NWETm, enlarged waist-normal triglycerides/normal waist-elevated triglycerides modified; HAQ-DI, health assessment questionnaire disability index; HDL-c, high-density lipoprotein cholesterol; hsCRP, high sensibility protein c reactive; HTGW, hypertriglyceridaemic waist; HTGWm, hypertriglyceridaemic waist modified; HUC, hyperuricaemia; LDL-c, low-density lipoprotein cholesterol; MetS, metabolic syndrome; MetSm, metabolic syndrome modified; NWNT, normal waist-normal triglycerides; NWNTm, normal waist-normal triglycerides modified; RA, rheumatoid arthritis; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; UA, uric acid.

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https://doi.org/10.1016/j.dsx.2018.11.053
1871-4021/

that the UA levels are increased in relation to the number of components of the metabolic syndrome (MetS) [11], as well as a predictive marker of MetS and coronary artery disease [7,12], comorbidities that represent great clinical interest in RA. The purpose of this study was to evaluate the presence of HTGW phenotype as a cardiometabolic risk parameter related to the presence of HUC and MetS in patients with RA.

## 2. Materials and methods

### 2.1. Study population

A total of 250 patients with RA (232 women and 18 men) classified according to the 2010 American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) criteria [13] were enrolled from the Rheumatology Department of General Hospital “Dr. Raymudo Abarca Alarcón ”, Chilpancingo, Guerrero, Mexico. We excluded patients with an overlapping syndrome (characteristics of two autoimmune connective tissue diseases present in the same patient), pregnancy, antecedents of cancer, epilepsy, chronic viral infections (hepatitis C or B virus or human immunodeficiency virus), or acute bacterial, viral, or fungal infections. We excluded patients with hypothyroidism, liver and kidney disease, cushing disease, family history of dislipidemia and drugs such as lipid lowering drugs, beta blockers, oral contraceptive pills, estrogens, progesterone, vitamin E and others drugs. The patients were recruited during the period from February 2016 to August 2017. The study was approved by the Research Ethics Committee of the Autonomous University of Guerrero, Mexico, and by the Ethics Committee of the General Hospital of Chilpancingo, Guerrero, Mexico. All patients agreed to participate and gave their informed consent in writing.

### 2.2. Clinical assessment

All of the patients were surveyed to obtain sociodemographic data. The clinical and treatment characteristics were evaluated during the consultation and from the clinical file. The 181 patients were treated with disease-modifying antirheumatic drugs (DMARDs), corticosteroids and nonsteroidal anti-inflammatory drugs at a stable during the 6 months prior to the study onset and 69 patients newly diagnosed without treatment. The treatment with DMARDs prescribed was methotrexate, chloroquine, sulfasalazine and leflunomide. The nonsteroidal anti-inflammatory drugs were diclofenac. The corticosteroids were the prednisone and metilprednisolone (intramuscular injection). The rheumatologist doctor performed a clinical evaluation and counted the number of inflamed and painful joints; the patient indicated the level of perception of health status and level of pain perception through a visual analogue scale.

Disease activity and disability were evaluated through the Disease Activity Score 28 (DAS28) and Spanish version of Health Assessment Questionnaire (HAQ-DI), respectively. Using a peripheral blood sample, clinical parameters were determined in all patients as follow: the erythrocyte sedimentation rate (ESR) was determined by the Wintrobe method. The high sensibility C reactive protein (hsCRP) was determined using immunoturbidimetry technique in the automatized reader COBAS C311 (Roche Diagnostics GmbH, Germany). Rheumatoid factor was evaluated using turbidimetry technique (Roche Diagnostics GmbH, Mannheim, Germany). The positivity was considering according to the kit was >20 UI/mL. Anti-CCPs anti-autoantibodies was determined using a commercial kit (DIASTAT anti-CCP de Axis-Shield, Dundee, United Kingdom) in the automatized equipment Multiskan FC Microplate Photometer (Thermo Scientific, Shangái). The positive values according to the semiquantitative kit was >5 U/mL.

### 2.3. Anthropometrical and blood pressure measurements

The weight and body mass index (BMI) was evaluated in light clothing and without shoes using bioelectrical impedance technique (Omron, IL, USA). Height was determined using a portable stadiometer (Seca 240, Hamburg, Ger-many). Waist circumference (WC) was measured at the level of the umbilicus, with the subject standing. Hip girth was measured at the maximum circumference of the buttocks. The body circumferences were measured by duplicated using a measuring tape with an accu-racy of ±0.1 cm (Seca 201, Hamburg). The blood pressure systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the left arm in duplicate at intervals of 5 min and after a minimum rest state of 5 min using an automated baumanometer (HEM-712C, Omron, IL, USA.

### 2.4. Biochemical measurements

Fasting (8 h overnight) blood samples were collected by venepuncture. The serum samples were obtained by centrifugation, and were stored at −20 °C until use. Fasting serum glucose, total cholesterol, triglycerides, high density lipoprotein (HDL-c), urea, creatinine and uric acid (UA) were certificated by colorimetric assays using reagents brand Wiener lab at a semi-automated equipment Cobas Miras (Roche Diagnostics GmbH, Germany). All laboratory equipments were calibrated and blinded duplicate samples were used. To determine the levels of low density lipoprotein cholesterol (LDL-c), the Friedewald formula was used: LDL-c (mg/dL) = [total cholesterol]-[HDL + triglycerides/5] [14].

### 2.5. Definitions

#### 2.5.1. Hypertension

The alteration of blood pressure was established according to the criteria to the Eight Joint National Commite on Prevention, Detection, Evaluation, and Treatment of high blood pressure. For the patients with normotension SBP as well as DBP were <120/80 mmHg. For the prehypertension, SBP and DBP were 120–139/80–89 mmHg. For the hypertension, SBP and DBP ≥140/90 mmHg was considered. Only 28 patients reported the use of pharmacological treatment based on angiotension-converting enzyme (ACE) inhibitors. Only 3 patients had combination with diuretics.

#### 2.5.2. Type 2 diabetes mellitus

Was defined according to the American Diabetes Associaton. Fasting hyperglycemia ≥126 mg/dL. A total of 20 patients had a diagnosis of type 2 diabetes mellitus (T2DM). Only 11 of them reported the use of metformine and the rest the combination with insulin or glibenclamide.

#### 2.5.3. Hyperuricaemia

The HUC was defined using two criteria: UA levels >6 mg/dL for women and >7 mg/dL for men [15], and UA levels >5.5 mg/dL for both genders [16].

#### 2.5.4. Metabolic syndrome

The MetS it was defined by the presence of three or more of the NCEP-ATP III criteria; abdominal obesity (waist ≥88 cm for women and for men ≥102 cm), SBP altered (≥130 mmHg) and/or DBP altered (≥85 mmHg), elevated triglycerides (≥150 mg/dL), low HDL-c (<40 mg/dL in men and <50 mg/dL in women), and high glucose fasting (≥100 mg/dL). In addition, the presence of MetS was defined using the modified NCEP-ATPIII criteria (MetSm), which established a waist circumference ≥80 cm for women and ≥90 cm for men as abdominal obesity, in populations of Asian descent [17].

*2.5.5. Hypertriglyceridaemic waist phenotype*

To assess the HTGW, the NCEP-ATP III criteria was used and the patients were classified into three groups: (1) NWNT (normal waist-normal triglycerides), where the values of waist circumference were <88 cm for women and <102 cm for men, and levels of triglycerides <150 mg/dL, (2) NWET/EWNT (normal waist-elevated triglycerides or enlarged waist-normal triglycerides) group, where there is normal waist and elevated serum triglycerides, or a high waist and normal serum triglycerides, and (3) HTGW (hypertriglyceridaemic waist) group, defined by an elevated waist ≥88 cm for women and ≥102 cm for men and serum triglycerides ≥150 mg/dL. The presence of modified HTGW (HTGWm) was also defined based on a waist circumference ≥80 cm for women and ≥90 cm for men, and values ≥ 150 mg/dL for serum triglycerides [4,17].

*2.5.6. Statistical analysis*

Statistical analysis was carried out using the softwares; Stata version 13.0 (StataCorp, College Station, TX, USA), SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) and GraphPad prism version 7.0 (GraphPad Software, San Diego, CA, USA). Categorical data were expressed as the number and proportions, compared using $X^2$ test. Continues variables were compared among groups by Kruskal–Wallis Test. ROC curves was constructed to determine the uric acid levels, waist circumference and triglyceride levels as test variables with more sensitivity and specificity for association with MetS and HUC. In all cases, the areas under the curve were calculated with the respective 95% confidence values and their p value adjusted for age. The association between the HTGW phenotype, HUC and MetS in its traditional NCEP/ATPIII versions and modified was tested using multivariable logistic regression models, with odds ratios (ORs) and 95% confidence intervals (CI) calculated. The values of $P < 0.05$ indicated statistical significance.

## 3. Results

We included 250 RA patients with an average age of 46 years. According to traditional NCEP/ATPIII criteria; 87 (34.8%) patients presented NWNT phenotype, 112 (44.8%) were classified as EWNT/NWET, and 51 (20.4%) belonged to the HTGW phenotype. According modified criteria; 46 (18.4%) patients were assigned to the NWNT, 124 (49.6%) were assigned to the EWNT/NWET, and 80 (32%) belonged to the HTGW phenotype modified.

### *3.1. Baseline characteristics of the RA patients across the HTGW phenotypes*

Table 1 the prevalence of HTGW phenotype increased by 12% with the modified criteria. The patients with HTGW and HTGWm showed increased BMI, SBP, glucose, total cholesterol, LDL-c, and levels of UA, as well as a higher prevalence of MetS and decreased HDL-c levels ($P < 0.001$). Hypertension was associated to HTGW phenotype in both versions ($P < 0.05$), while T2DM was associated with the HTGWm ($P$ 0.011). The pharmacological treatment with the hypertension and T2DM not associated with HTGW or HTGWm phenotypes (Table 1). The HTGW and HTGWm phenotypes were not associated with clinical, serologic markers and treatment antirheumatic in RA patients (Table 2).

### *3.2. Prevalence of hyperuricaemia in the two subgroups*

The HUC frequency (UA >6/7 mg/dL) was 14.1%, increasing by 9% when levels of UA >5.5 mg/dL were considered (23%). In patients with HTGW and HTGWm, the frequency of HUC was similar (Table 1). As show in Fig. 1, the patients with NWET/EWNT, HTGW and MetS showed significantly higher levels of UA, with respect to those with NWNT (Fig. 1a). Nevertheless, the UA levels were similar between patients with HTGWm and MetSm (Fig. 1b).

### *3.3. Receiver operating characteristic (ROC) curves for the HTGW components and UA levels as diagnostic markers for HUC and MetS*

In the ROC curves, the discriminatory power of triglycerides and waist circumference in the prediction of HUC (>6/7 mg/dL) were AUC 0.736 for triglycerides, and AUC 0.681 for waist circumference (Fig. 2a) and for HUC (>5.5 mg/dL) were AUC 0.714 for triglycerides, and AUC 0.652 for waist circumference (Fig. 2b). Furthermore, the discriminatory power of UA in the prediction of MetS were AUC 0.599 (Fig. 2c), and AUC 0.678 for MetS modified (Fig. 2d).

### *3.4. Association between HTGW phenotype and hyperuricaemia*

To further investigate the relationship between HTGW phenotype and HUC, a multivariate analysis was performed. RA patients with the HTGW phenotype presented 5.70 and 6.14 times more likely of having HUC (>6/7 mg/dL and >5.5 mg/dL, respectively). As well as, the patients with MetS showed significantly more likely of having HUC defined by both criteria. The HTGW was the most closely related parameter to HUC in comparison to components of MetS (Table 3).

## 4. Discussion

The assessment of metabolic disorders in RA patients is of great clinical interest, given that the chronic inflammatory process and pharmacological treatment increases metabolic risk [18,19]. HTGW has been suggested as a marker of metabolic disease [20] and CVR [21,22]. In a study conducted by Núñez-Cortés et al. [23] in patients included in a national registry of hypertriglyceridaemia by the Spanish Society of Arteriosclerosis, the frequency of HTGW was 50%, twice that found in this study. In RA patients, a good clinical and therapeutic management was shown to reduce clinical disease activity and improve the metabolic state. In this study, HTGW was shown to be in close agreement with the presence of MetS; in clinical practice, HTGW could be considered a tool to assess the metabolic risk in patients with RA. In Mexican patients with RA, the prevalence of MetS ranges between 11.3% and 17.5% [24]; in this study, the prevalence was higher (44% and 55.2%) and similar to that reported in patients with RA in Peru [25], Greece [26] and Turkey [27]. The differences could be explained by the use of different criteria in the definition and classification of MetS, as well as the clinical characteristics of patients.

On the other hand, the presence of HUC was high in patients with HTGW and MetS; similar Results were described by Sari et al. [7], who suggested that increased levels of UA are predictor markers of MetS, and related to coronary artery disease and inflammatory disorders. In other populations without RA, the frequency of HUC is variable; Chang et al. reported a HUC prevalence (UA >7 mg/dL) of 46.2% in a veteran population [28], while Lohsoonthorn et al. [29] reported a prevalence in a Thai population that was lower (10.6%; UA >6/<7 mg/dL). The cutting value of UA to define HUC has not been fully established. In this study, the HUC, defined by two different values, was associated with the presence of HTGW and MetS. A study conducted in a population without RA reported that those with HTGW had three or more metabolic alterations and excess visceral adipose tissue [21]. It has been shown that the accumulation of visceral fat can generate adverse effects in the metabolism of UA in the clinically healthy population [30]. In a

**Table 1**
Sociodemographic and metabolic characteristics of study participants across HTGW phenotype groups.

| Variables | Total ($n = 250$) | NWNT ($n = 87$) | EWNT/NWET ($n = 112$) | HTGW ($n = 51$) | *P* value | NWNTm ($n = 46$) | EWNTm/NWETm ($n = 124$) | HTGWm ($n = 80$) | *P* value |
|---|---|---|---|---|---|---|---|---|---|
| Gender (female/male)[a] | 232/18 (93/7) | 78/9 (90/10) | 104/8 (93/7) | 50/1 (98/2) | 0.18 | 42/4 (91/9) | 117/7(94/6) | 73/7 (91/9) | 0.64 |
| Age (year)[b] | 46 (24–71) | 40 (22–74) | 47 (26–70) | 48 (27–65) | 0.07 | 34 (21–74) | 43 (26–71) | 49 (31–66) | 0.002 |
| Current smoking status[a] | 8 (3.2) | 1 (1.2) | 4 (3.6) | 3 (5.9) | 0.29 | 1 (2.2) | 1 (0.8) | 8 (7.5) | 0.03 |
| Current drinking alcohol status[a] | 9 (3.6) | 4 (4.6) | 3 (2.7) | 2 (3.9) | 0.76 | 1 (2.2) | 5 (4.0) | 3 (3.8) | 0.84 |
| Waist circumference (cm)[b] | 87 (70–113) | 80 (67–90) | 91 (75–115) | 98 (89–114) | <0.001 | 75 (65–84) | 89 (75–113) | 94 (82–113) | <0.001 |
| BMI (kg/m$^2$)[b] | 26.9 (19.8–37.5) | 23.7 (18–28) | 28.2 (21.5–38.2) | 31.3 (25.9–37.6) | <0.001 | 21.7 (17.6–26) | 27.35 (21.61–37.6) | 29 (23.4–37.6) | <0.001 |
| Glucose (mg/dL)[b] | 91 (74–142) | 86 (72–119) | 93 (74–142) | 98 (75–155) | <0.001 | 85 (74–110) | 91.5 (74–146) | 96.5 (71.5–147.5) | <0.001 |
| Cholesterol (mg/dL)[b] | 168 (107–254) | 146 (93–199) | 175 (117–260) | 186 (136–271) | <0.001 | 139 (87–196) | 167 (112–246) | 187.5 (141.5–270) | <0.001 |
| Triglycerides (mg/dL)[b] | 133 (67–275) | 103 (57–144) | 140 (79–275) | 193 (152–358) | <0.001 | 94.5 (57–143) | 121.5 (70–223) | 195 (152.5–344.5) | <0.001 |
| HDL cholesterol (mg/dL)[b] | 36.6 (20.7–60.5) | 36.5 (20.8–62.5) | 39.5 (22.8–63.6) | 32.6 (18.7–55.5) | 0.025 | 36.9 (21.2–60.5) | 38.8 (23.1–63.8) | 34.7 (18.1–54.4) | 0.06 |
| LDL cholesterol (mg/dL)[b] | 102.5 (53.9–169.8) | 88.7 (49.9–134) | 105.1 (61.4–180.5) | 111.4 (63.6–185) | <0.001 | 86.8 (35.3–134.6) | 102.1 (59.3–162) | 113.4 (66.5–185.8) | <0.001 |
| MetS[a] | 110 (44.0) | 3 (3.5) | 56 (50.0) | 51 (100) | <0.001 | 1 (2.2) | 45 (36.3) | 64 (80) | <0.001 |
| MetSm[a] | 138 (55.2) | 16 (18.4) | 71 (63.4) | 51 (100) | <0.001 | 1 (2.2) | 58 (46.8) | 79 (98.8) | <0.001 |
| Urea (mg/dL)[b] | 28 (16–52) | 27 (15–54) | 28 (16–41) | 28 (20–73) | 0.33 | 28 (16–62) | 27.5 (15–43) | 28 (17–59) | 0.46 |
| Creatinine (mg/dL)[b] | 0.7 (0.5–1.0) | 0.7 (0.5–1.0) | 0.7 (0.5–0.9) | 0.7 (0.5–1.1) | 0.54 | 0.7 (0.5–1.1) | 0.65 (0.5–0.9) | 0.7 (0.5–1.05) | 0.36 |
| Uric acid (mg/dL)[b] | 4.6 (3–7.7) | 4.2 (2.6–6.7) | 4.7 (3.3–7.9) | 5.1 (3.4–8.4) | <0.001 | 4.2 (2.8–6.7) | 4.4 (2.8–6.3) | 5.2 (3.8–9.2) | <0.001 |
| Hyperuricaemia (>6 y > 7 mg/dL)[a] | 35 (14.1) | 3 (3.5) | 16 (14.6) | 16 (31.4) | <0.001 | 3 (6.5) | 8 (6.6) | 24 (30) | <0.001 |
| Hyperuricaemia (>5.5 mg/dL)[a] | 57 (23.0) | 8 (9.2) | 26 (23.6) | 23 (45.1) | <0.001 | 6 (13.0) | 16 (13.1) | 35 (43.8) | <0.001 |
| Prehypertension | 86 (34.7) | 22 (25.3) | 45 (40.2) | 19 (38.8) | 0.008 | 7 (15.2) | 44 (35.5) | 35 (44.9) | 0.001 |
| Hypertension | 61 (24.6) | 16 (18.4) | 30 (26.8) | 15 (30.6) | | 8 (17.4) | 35 (28.2) | 18 (23.1) | |
| Type 2 diabetes mellitus | 20 (8.0) | 8 (9.2) | 10 (8.9) | 2 (3.9) | 0.48 | 0 (0) | 16 (12.9) | 4 (5.0) | 0.011 |

$P < 0.05$ is considered statistically significant.

*BMI* body mass index, *DBP* diastolic blood pressure, *EWNT/NWET* enlarged waist-normal triglycerides/normal waist-elevated triglycerides, *EWNT/NWETm* enlarged waist-normal triglycerides/normal waist-elevated triglycerides modified, *HDL-c* high-density lipoprotein cholesterol, *HTGW* hypertriglyceridaemic waist, *HTGWm* hypertriglyceridaemic waist modified, *LDL-c* low-density lipoprotein cholesterol, *MetS* metabolic syndrome, *MetSm* metabolic syndrome modified, *NWNT* normal waist-normal triglycerides, *NWNTm* normal waist-normal triglycerides modified, *SBP* systolic blood pressure.

[a] Data are expressed as the n(%) using $X^2$ test.

[b] Data are expressed as the median using percentiles 5–95 (Kruskal Wallis test).

**Table 2**
Clinical and treatment characteristics of study participants across HTGW phenotype groups.

| Variables | Total (n = 250) | NWNT (n = 87) | EWNT/NWET (n = 112) | HTGW (n = 51) | P value | NWNTm (n = 46) | EWNTm/NWETm (n = 124) | HTGWm (n = 80) | P value |
|---|---|---|---|---|---|---|---|---|---|
| Time of evolution (years)[b] | 7 (1–26) | 7 (1–22) | 8 (1–26) | 5 (1–30) | 0.27 | 8 (0.8–15) | 8 (1–25) | 6 (1–30) | 0.52 |
| HAQ-DI (Units)[b] | 0.3 (0–1.5) | 0.3 (0–1.5) | 0.3 (0–1.7) | 0.4 (0–1.3) | 0.70 | 0.25 (0–1.2) | 0.3 (0–1.8) | 0.1 (0–1.3) | 0.08 |
| DAS28-ESR (Units)[b] | 3.6 (1.9–7.3) | 3.6 (2.0–7.9) | 3.6 (1.9–7.2) | 3.6 (1.9–7.4) | 0.85 | 3.2 (2.0–6.8) | 3.9 (2.0–7.3) | 3.6 (1.9–7.4) | 0.13 |
| ESR (mm/h)[b] | 31 (9–55) | 28 (10–55) | 31 (9–55) | 32 (14–55) | 0.58 | 26 (10–52) | 30 (7–56) | 33 (10–55) | 0.26 |
| hsCRP (mg/L)[b] | 6.9 (0.1–60.2) | 5.9 (0.6–59.5) | 6.7 (0.1–60.2) | 9.4 (0.1–63.7) | 0.49 | 5.7 (0.5–132.0) | 7.5(0.6–60.2) | 7.1 (0.1–33.8) | 0.21 |
| Rheumatoid factor (positive)[a] | 185 (84.9) | 66 (82.5) | 79 (84.0) | 40 (90.9) | 0.43 | 38 (88.4) | 88 (80.0) | 59 (90.8) | 0.12 |
| Anti-CCPs (positive)[a] | 213 (85.9) | 76 (88.4) | 94 (84.7) | 43 (84.3) | 0.71 | 40 (88.9) | 106 (86.2) | 67 (83.8) | 0.72 |
| Methotrexate[a] | 173 (69.2) | 58 (66.7) | 83 (74.1) | 32 (62.8) | 0.28 | 32 (69.6) | 91 (73.4) | 50 (62.5) | 0.25 |
| Cholroquine[a] | 133 (53.2) | 43 (49.4) | 67 (59.8) | 23 (45.1) | 0.14 | 27 (58.7) | 70 (56.5) | 36 (45.0) | 0.19 |
| Sulfasalazine[a] | 62 (24.8) | 21 (24.1) | 31 (27.7) | 10 (19.6) | 0.53 | 9 (19.6) | 38 (30.7) | 15 (18.8) | 0.10 |
| Leflunamide[a] | 23 (9.2) | 10 (11.5) | 10 (8.9) | 3 (5.9) | 0.54 | 4 (8.7) | 14 (11.3) | 5 (6.3) | 0.47 |
| Diclofenac[a] | 88 (35.2) | 25 (28.7) | 44 (39.3) | 19 (37.3) | 0.28 | 13 (28.3) | 47 (37.9) | 28 (35.0) | 0.50 |
| Prednisone[a] | 144 (57.6) | 49 (56.3) | 69 (61.6) | 26 (51.0) | 0.42 | 25 (54.4) | 78 (62.9) | 41 (51.3) | 0.22 |
| Methylprednisolone[a] | 93 (37.2) | 32 (36.8) | 44 (39.3) | 17 (33.3) | 0.76 | 17 (37.0) | 50 (40.3) | 26 (32.5) | 0.52 |

$P < 0.05$ is considered statistically significant.
*Anti-CCPs* anti-cyclic citrullinated peptide antibodies, *DAS28* disease activity score 28, *ESR* erythrocyte sedimentation rate, *EWNT/NWET* enlarged waist-normal triglycerides/normal waist-elevated triglycerides, *EWNT/NWETm* enlarged waist-normal triglycerides/normal waist-elevated triglycerides modified, *HAQ-DI* health assessment questionnaire disability index, *HTGW* hypertriglyceridaemic waist, *hsCRP* high sensibility protein c reactive, *HTGWm* hypertriglyceridaemic waist modified, *NWNT* normal waist-normal triglycerides, *NWNTm* normal waist-normal triglycerides modified.
[a] Data are expressed as the n(%) using $X^2$ test.
[b] Data are expressed as the median using percentiles 5–95 (Kruskal Wallis test).

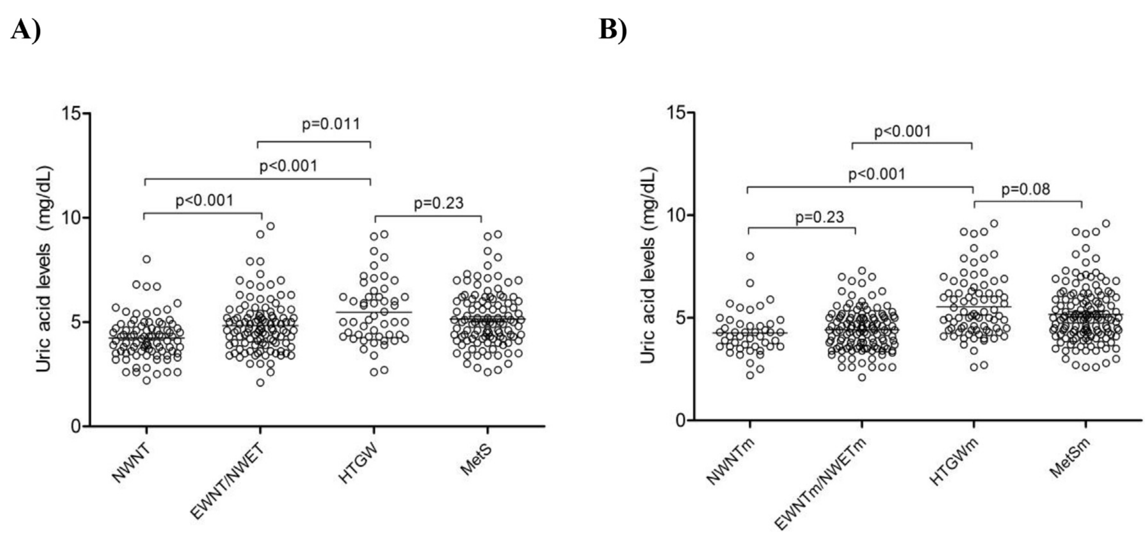


**Fig. 1.** Distribution of uric acid levels according to study groups. a) Distribution of uric acid levels in normal criteria for the HTGW phenotype, HUC and MetS. b) Distribution of uric acids levels in modified criteria HTGW phenotype, HUC and MetS. Mann Whitney *U* test, $p < 0.05$ is considered statistical significant. Data proved in medias (p5-p95). Circles illustrate Results of individual samples. Horizontal bars illustrate median (large bar). *EWNT/NWET* enlarged waist-normal triglycerides/normal waist-elevated triglycerides, *EWNT/NWETm* enlarged waist-normal triglycerides/normal waist-elevated triglycerides modified, *HTGW* hypertriglyceridaemic waist, *HTGWm* hypertriglyceridaemic waist modified, *MetS* metabolic syndrome, *MetSm* metabolic syndrome modified, *NWNT* normal waist-normal triglycerides, *NWNTm* normal waist-normal triglycerides modified.

study conducted by Yamada et al. [31], they observed that the accumulation of visceral fat in the liver is associated with the presence of HUC, independent of other fatty deposits and insulin levels. Tamba et al. [32] reported that visceral fat accumulation is associated with increased levels of UA and low adiponectin concentration in the adult population, and Fruehwald-Schultes et al. [33] reported that serum leptin levels are associated with UA levels, suggesting that this is one of the factors related to obesity in the presence of HUC. Therefore, in patients with RA, the study of adipocytokines and their relationship with HUC and cardiometabolic risk markers is of interest.

In addition, it has been suggested that the UA levels increase in the presence of an altered lipid profile [34]. In this study we observed triglycerides; the HTGW phenotype component and the MetS are associated with both criteria of HUC in RA patients. It has been suggested that there is a relationship between xanthine oxidase and triglycerides in hypertriglyceridemic patients of type IV, where HUC is common [35]. Chang et al. [28] reported the relationship between HUC and high triglyceride levels, increased waist circumference and low levels of HDL-c in veteran's population.

In this study, HUC was associated with the presence of MetS, as well as with its individual components. Choi et al. [36] and Rho et al. [37] reported increased of UA levels and HUC associated with the number of MetS components. Liu et al. [9] reported that UA levels above the fourth quartile are related to the presence of MetS in both genders; similarly, Lohsoonthorn et al. [29] observed that the UA levels are associated with the presence of MetS, and that UA levels >4.6 mg/dL relate to the MetS presence in the female gender.

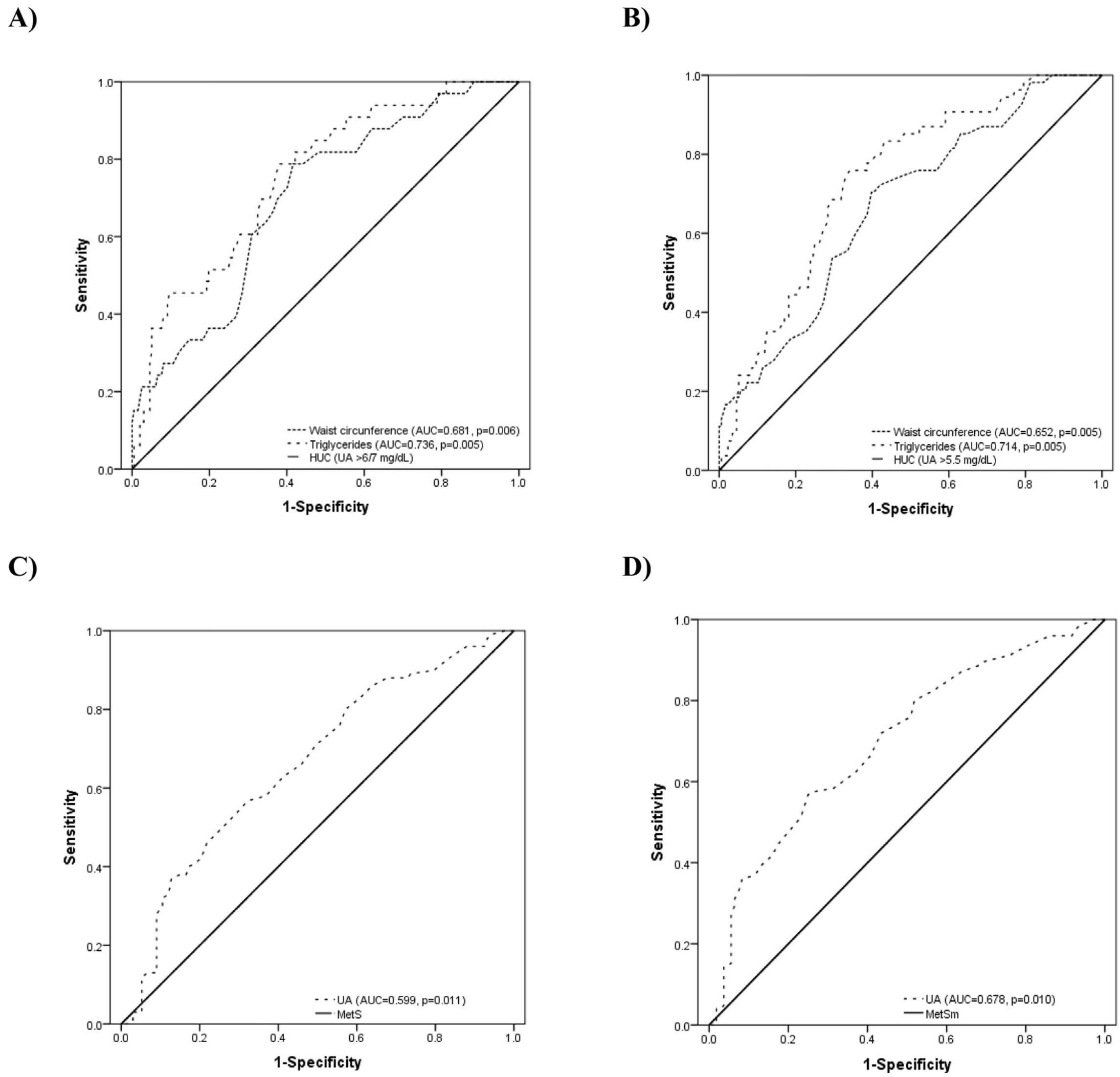


**Fig. 2.** ROC curves of the HTGW components a uric acid levels in HUC and MetS. A) HUC (UA >6/7 mg/dL), B) HUC (UA >5.5 mg/dL), C) MetS, D) MetSm. Adjusted by age. *AUC* area under curve, *HUC* hiperuricaemia, *MetS* metabolic syndrome, *MetSm* metabolic syndrome modified form, *UA* uric acid.

**Table 3**
Association between HTGW phenotype, MetS components and HUC in RA patients.

| Variables | HUC (UA >6/>7 mg/dL) | | | HUC (UA >5.5 mg/dL) | | |
|---|---|---|---|---|---|---|
| | OR | CI 95% | *P* value | OR | CI 95% | *P* value |
| EWNT/NWET | 6.22 | 1.57–24.59 | 0.009 | 5.86 | 1.86–18.43 | 0.002 |
| HTGW | 5.70 | 2.49–12.96 | <0.001 | 6.14 | 2.94–12.82 | <0.001 |
| EWNT/NWETm | 0.97 | 0.3–4.0 | 0.97 | 1.10 | 0.35–3.41 | 0.86 |
| HTGWm | 6.90 | 3.07–15.51 | <0.001 | 6.60 | 3.26–13.25 | <0.001 |
| Waist circumference (≥102/88 cm) | 4.17 | 1.70–10.2 | 0.002 | 3.16 | 1.54–6.47 | 0.002 |
| Waist circumference (≥90/80 cm) | 3.66 | 1.19–11.18 | 0.023 | 2.05 | 0.91–4.61 | 0.08 |
| SBP (≥130 mmHg) | 2.26 | 1.06–4.81 | 0.034 | 2.25 | 1.17–4.32 | 0.014 |
| DBP (≥85 mmHg) | 0.91 | 0.32–2.59 | 0.86 | 0.96 | 0.39–2.33 | 0.93 |
| Glucose (≥100 mg/dL) | 1.96 | 0.90–4.26 | 0.08 | 2.10 | 1.07–4.13 | 0.03 |
| Triglycerides (≥150 mg/dL) | 4.70 | 2.08–10.4 | <0.001 | 6.00 | 2.9–12.33 | <0.001 |
| HDL cholesterol (<40/<50 mg/dL) | 0.70 | 0.28–1.72 | 0.43 | 1.45 | 0.59–3.6 | 0.41 |
| MetS | 3.50 | 1.54–7.94 | 0.003 | 5.70 | 2.66–12.23 | <0.001 |
| MetSm | 5.90 | 2.16–16.07 | 0.001 | 8.60 | 3.44–21.33 | <0.001 |

Model adjusted by gender, time evolution of disease and treatment by DMARDs.
$P < 0.05$ is considered statistically significant.
*OR* Odds ratio, *CI* 95% Confidence Interval, *DBP* blood pressure diastolic, *DMARDs* disease-modifying antirheumatic drugs, *EWNT/NWET* enlarged waist-normal triglycerides/ normal waist-elevated triglycerides, *EWNT/NWETm* enlarged waist-normal triglycerides/normal waist-elevated triglycerides modified, *HDL-c* high-density lipoprotein cholesterol, *HTGW* hypertriglyceridaemic waist, *HTGWm* hypertriglyceridaemic waist modified, *MetS* metabolic syndrome, *MetSm* metabolic syndrome modified, *NWNT* normal waist-normal triglycerides, *NWNTm* normal waist-normal triglycerides modified, *RA* rheumatoid arthritis, *SBP* systolic blood pressure, *UA*, uric acid levels.

In an Iranian population with MetS, an average UA value of 5.57 mg/dL has been found in men and 5.54 mg/dL in women [11]. In this study, in addition to the parameters described by Chang et al. [28], an association was found with SBP. In this regard, Liu et al. [9] reported that HUC increases the risk of presenting altered blood pressure and MetS, especially in women, a gender that is mostly affected by RA. In the Chinese population, it has been reported that HUC tends to increase the risk of MetS in young women [38].

In this study, HUC was consistently associated with HTGW. A transversal study revealed that the presence of HTGW increases the risk of developing a cardiovascular events to 10 years, so the HTGW is an early marker of CVR to be implemented as a simple and inexpensive tool [22], since this only requires anthropometric exploration and determining a biochemical parameter (triglycerides), both of which are parameters with feasibility and periodic evaluation in the patient with RA. As well as being considered a predictive marker of CVR, HTGW must be considered in the screening of high-risk populations, such as in patients with RA in whom CVD represents the main cause of morbidity and mortality. The Results of this study show the close relationship between HUC, HTGW and MetS in a comparative analysis, meaning that HTGW can be considered a marker in the evaluation of metabolic and CVR in patients with RA, which will increase its validity for the development of other replication studies and their implementation in the clinical evaluation of patients with RA. Finally, some limitations of our study should be considered, we could not exclude completely the influence of dietary factors, and others endocrine disorders related on UA levels.

## 5. Conclusion

The presence of HTGW is associated with the presence of HUC and MetS in patients with RA from southern Mexico, so it can represent a predictor of CVR; it is simple, inexpensive and useful in the screening of metabolic comorbidities in rheumatic patients.

## Compliance with ethical standards

*Financing*

The authors declare that they have not received any funding to carry out this study.

*Confidentiality of the data*

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

*Conflict of interests*

The authors declare that they have no conflicts of interest.

*Ethical approval*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki declaration.

## Acknowledgements

Special thanks to the patients, for allowing us to use them as subjects to investigate in the present study. Also, thanks go to the group of collaborators in the multidisciplinary team who contributed their knowledge and support for the management of and integral approach to these patients.

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