Thyroid hormone levels associate with insulin resistance in obese women with metabolic syndrome in Saudi Arabia: A cross-sectional study

Manal Abdulaziz Binobead¹, Nawal Abdullah Al Badr¹, Wahidah Hazzaa Al-Qahtani¹, Sahar Abdulaziz AlSedairy¹, Tarfa Ibrahim Albrahim², Maha Hussain Alhussain¹, Tahani Ali Aljurbua¹, Shaista Arzoo¹, Wedad Saeed Al-Qahtani³

¹ College of Food Science & Agriculture, Department of Food Science & Nutrition, King Saud University, Riyadh, Saudi Arabia.

² Department of Health Sciences, College of Health and Rehabilitation Sciences. Princess Nourah bint Abdulrahman University

³ Naif Arab University for Security Sciences, Saudi Arabia

Corresponding Author;

Wedad Saeed Al-Qahtani

Naif Arab University for Security Sciences, Faculty of Forensic Sciences, Forensic Biology

Department

Email;

walqahtani@nauss.edu.sa

dr.wedad.alqahtani@gmail.com

Acknowledgements

The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for funding this work through the Research Project No R6-17-03-65.

Abstract

Background

The obesity epidemic is a pressing global health concern, as obesity rates continue to climb worldwide. The current study was aimed mainly to evaluate the correlation between thyroid hormones and homeostatic model assessment of insulin resistance in Saudi obese women with metabolic syndrome.

Methods

100 obese women aged 25 to 55 years were clinically evaluated, from which 72 women were diagnosed with the metabolic syndrome and 28 without metabolic syndrome. Insulin resistance was quantified using the homeostatic model assessment of insulin resistance method and the resulting values were analyzed for association with demographic, clinical, and metabolic parameters.

Results

This analysis revealed that body mass index, systolic blood pressure, and biochemical parameters and fasting insulin showed statistically higher levels in the group with metabolic syndrome compared to the group without metabolic syndrome. Similarly, values of waist circumference, fat ratio, cholesterol, free thyroxine, free triiodothyronine and homeostatic model assessment of insulin resistance results were higher in the group with metabolic syndrome as compared to the group without metabolic syndrome. Correlation analysis revealed positive association of thyroid-stimulating hormone with waist circumference ($P=0.01$), total cholesterol ($P=0.002$), fasting insulin ($P=0.03$) and homeostatic model assessment of insulin resistance results ($P<0.01$), and negatively associated with diastolic blood pressure ($P=0.013$) and age ($P=0.05$). Free thyroxine was positively associated with triglyceride level ($P=0.003$) and negatively associated with homeostatic model assessment of insulin resistance values ($P=0.035$) and fasting insulin. Free triiodothyronine was positively associated with body mass index ($P=0.032$) and waist circumference ($P=0.006$) and negatively with age ($P=0.004$) and total cholesterol ($P=0.001$).

Homeostatic model assessment of insulin resistance test revealed elevated level with positive association of body mass index, waist circumference, biochemical parameters and

thyroid-stimulating hormone in insulin resistant obese women. Higher level of free triiodothyronine was found to be associated with low insulin sensitivity.

Keywords: Metabolic syndrome, insulin resistance, diabetes, thyroid hormone, obesity

Introduction

The obesity and overweight are associated to the risk of health complications and premature death, obesity is the greatest contributing factor underlying the metabolic syndrome (MetS) (Danaei et al., 2014). MetS is a chronic medical condition manifested by a cluster of symptoms (e.g., low high-density lipoprotein cholesterol (HDL-C) levels, high blood pressure (BP), high triglyceride (TG) levels, insulin resistance (IR), and other anthropometric and biochemical factors) that are associated with developing cardiovascular disease and type 2 diabetes mellitus (Ford et al., 2005). A precursor to type 2 diabetes. IR basically refers to the inability of insulin to perform its function at the optimum concentration required for its biological activity (Harris et al., 1998; Ferrannini, 2004). This causes responsible for this inability can range from defective glucose output in the liver to impaired insulin uptake in the muscle (Farasat et al., 2011).

Healthy thyroid activity is required to maintain the overall health of an individual. Several studies have described the effect of thyroid hormones on body mass index (BMI). Hypothyroidism leads to weight gain, while hyperthyroidism causes weight loss (Hoogwerf and Nutall, 1984). Moreover, it has also been established that obesity affects thyroid gland function (Topsakal et al., 2012). Previous studies have associated thyroid hormones with insulin activity, toward regulating the metabolism of glucose; the dysregulation of this pathway contributes to IR (Ravi and Gokaldas, 2015). Thyroid hormones regulated a variety of proteins involved in

maintaining insulin sensitivity (Klieverik et al., 2009). The loss of insulin sensitivity, IR, is associated with obesity and has been used as a predictor of developing cardiovascular disease and type 2 diabetes (Naslund et al., 2000). Multiple studies have evidenced the cooperative relationship between thyroid hormones and insulin in glucose metabolism (Lacobellis et al., 2005; Chakarabarti et al., 2007). Maintaining glucose homeostasis involves the complex interplay between physiological pathways that regulate insulin secretion and modulate its activity (Farasat et al., 2011). The American Association of Clinical Endocrinologists (AACE) has provided guidelines for the diagnosis of abnormal thyroid function and for the treatment of thyroid dysfunction in patients with abnormal serum levels of thyroid-stimulating hormone (TSH) (Gharib et al., 2004). The possible role of TSH in adipogenesis and IR has already been established (Bastemir et al., 2007). Among its various metabolic effectors, WC and BMI correlate positively with serum TSH levels (Knudsen et al., 2005); however, the relationship between IR and TSH remains largely unexplored, particularly in the Saudi, female population affected by MetS.

Therefore, the aim of this cross-sectional study is to identify associations between TSH, IR, and other clinically-relevant metrics in obese women with and without MetS in Saudi Arabia. The objectives of this study include: 1) to evaluate the anthropometric, clinical, and biochemical characteristics of the study subjects; 2) to analyze these characteristics for correlations with insulin sensitivity level; 3) to detect associations between TSH levels and the subjects' clinical and biochemical characteristics, MetS diagnosis, and insulin sensitivity level.

Materials and Methods

Study subjects

The analysis was carried out on 163 obese and overweight women aged 25 to 55 years. All of the patients had BMI ≥ 25 kg/m². The presence of medical conditions was assessed

through self-report. A pre-structured and pre-tested questionnaire were used to gather demographic information and personal and family medical history. Informed consent was obtained from all participants.

Inclusion criteria

This study included women aged 25 to 55 years with BMIs over 25 kg/m² (Fig. 1).

Exclusion criteria

Subjects with a history of smoking, polycystic ovary syndrome, chronic renal failure, thyroid disease, chronic hepatopathy, or cancer as well as subjects taking antihypertensive drugs and statins, contraceptive drugs, hormone replacement therapy, any medications known to interfere with glucose and/or insulin secretion and/or metabolism were excluded from the study (Fig. 1).

Demographic data

A pre-structured and pre-tested questionnaire was used to gather self-reported demographic information and individual and familial medical history.

Ethical considerations

Informed consent was orally obtained from all participants before they gave voluntary consent for this study and approved by IRB.

Anthropometric measurements

Anthropometric measurements were carried out three times by a single tester.

Height and weight

Height was measured without shoes and using a stadiometer. Body weight was morning determined in lightweight clothing, with a digital scale.

Body mass index (BMI)

BMI was calculated as the weight (kilograms) divided by the square of height (meters).

Waist circumference (WC)

Subject's WC was measured using a flexible measuring tape, midway between the xiphoid and the umbilicus during the mid-inspiratory phase.

Blood pressure (BP)

Two BP measurements were taken with the subject in the seated position at a 2- to 3-minute interval, after resting for at least 15 minutes. The average of these two readings was used for all patients.

Biochemical parameters

Blood samples were drawn after an overnight fast. Serum samples were analyzed for fasting blood glucose (FBG), TG, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) using commercially-available kits (Beckman-Coulter, CITY, STATE, USA). Serum insulin concentration was determined using an electrochemiluminescence-based assay (Immulite 2000, CITY, STATE, USA). Serum FT₄, FT₃, and TSH levels were also determined by electrochemiluminescence-based immunoassay (Roche Diagnostics, CITY, Germany).

The homeostatic model assessment (HOMA) ratio formula was used to quantify IR (Mathews et al., 1985).

$$\text{HOMA-IR} = [\text{fasting plasma insulin } (\mu\text{IU/ml}) \times \text{fasting plasma glucose (mmol/l)}] / 22.5$$

A HOMA-IR cut-off value chosen was 2.7 (> 2.7 resistant, < 2.7 sensitive).

Diagnosis of metabolic syndrome (MetS)

MetS was diagnosed according to standard protocol (Grundy et al., 2005) based on the presence of the following criteria: 1) TG $\geq$ 150 mg/dL; 2) LDL-C < 130 mg/dL; 3) HDL-C < 40 mg/dL; 4) TC < 200 mg/dL; 5) FBS $\geq$ 100 mg/dL; 6) SBP $\geq$ 130 mmHg; 7) DBP $\geq$ 85 mmHg; 8)

WC > 80 cm; 9) TSH > 2.5 IU/mL. Subjects with levels over the cut-off values were considered as MetS+ and subjects with levels under the cut-off values were considered to be MetS-.

Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) software package v25 (IBM, Chicago, IL, USA). Statistical comparisons between the MetS+ and MetS- groups were achieved with the one-way analysis of variance (ANOVA). Significance assessments were carried out using Duncan's new multiple range test. Values are expressed as means and standard deviations. We used hierarchical cluster analysis to assess the relationship between TSH levels and HOMA-IR values. Each experiment was repeated at least three times. A *P*-value of less than 0.05 was regarded as statistically significant.

Results

Of the 163 individuals considered, 63 were eliminated based on exclusion criteria (Fig. 1). The study population consisted of the remaining 100 obese (BMI > 25 kg/m²) women aged 25 to 55 years. Of these, 72 women were diagnosed as MetS+ and the remaining 28 were MetS-. The anthropometric and biochemical characteristics are presented in Table 1. BMI, SBP, TC, TG, HDL-C, FBP, TSH, and fasting insulin levels were statistically higher in the MetS+ group than the MetS- group. Similarly, the values for WC, fat ratio, LDL-C, FT₄, FT₃, and HOMA-IR were higher in the MetS+ group than the MetS- group; however, these differences were not statistically significant.

Based on the Pearson's correlation coefficients (Table 2), TSH positively associated with WC (*P* = 0.01) and TC (*P* = 0.002) and negatively associated with diastolic blood pressure (DBP) (*P* = 0.013) and age (*P* = 0.05). TSH also positively associated with insulin (*P* = 0.03) and HOMA-IR (*P* < 0.01). FT₄ positively associated with TG level (*P* = 0.003) and with HOMA-IR

value ($P = 0.035$). FT_3 positively associated with BMI ($P = 0.032$) and WC ($P = 0.006$) and negatively with age ($P = 0.004$) and TC ($P = 0.001$).

The comparison between insulin-sensitive and -resistant women in terms of the clinical and metabolic characteristics is presented in Figure 2. Using a cut-off value of 2.7 for HOMA-IR (> 2.7 resistant, < 2.7 sensitive), BMI, WC, TC, TG, LDL-C, FBS, and TSH were higher in the resistant group than the sensitive one. The positive association between IR and BMI ($P < 0.001$) and WC ($P < 0.05$) was statistically significant. Similarly, TSH was significantly associated with IR ($P = 0.03$). Higher FT_3 level associated with low levels of insulin sensitivity.

Furthermore, hierarchical cluster analysis grouped the clinical and metabolic data according to HOMA-IR values and revealed statistically significant associations between these groups (Fig. 3).

186 Table 1. Anthropometric and biochemical characteristics (data are given as a mean and standard
187 deviation)

Variables	MetS+	MetS-	<i>P</i> -value
	(<i>n</i> = 72)	(<i>n</i> = 28)	
	(<u>mean</u> ± SD)	(<u>mean</u> ± SD)	
Age (years)	33.12±9.06	28.64±8.39	NS
BMI (kg/m ²)	32.12±4.89	29.41±5.98	< 0.05
WC (cm)	89.38±7.93	80.44±2.34	NS
Fat ratio	39.24±6.60	24.62±4.35	NS
SBP (mmHg)	132.12±9.48	112.10±10.91	< 0.001
DBP (mmHg)	88.34±8.43	78.78±4.31	NS
TC (mg/dl)	234.67±9.79	193.94±9.75	< 0.001
TG (mg/dl)	167.83±8.90	151.41±8.26	< 0.001
HDL-C (mg/dl)	34.27±7.08	58.21±4.33	< 0.05
LDL-C (mg/dl)	130.42±11.37	125.72±11.45	NS
FBG (mg/dl)	109.55±10.47	94.70±8.12	< 0.001
TSH (mIU/l)	2.38±1.52	1.38±1.02	< 0.05
FT ₄ (pmol/l)	11.99±2.81	10.56±2.46	NS
FT ₃ (pmol/l)	6.22±1.70	5.47±2.47	NS
Fasting insulin (μIU/ml)	12.42±5.09	5.10±1.42	< 0.05
HOMA-IR	5.14±2.13	1.61±1.02	NS

188

189 Table 2. Pearson correlation coefficients (r) of TSH, FT₄, and FT₃ with demographic,
190 anthropometric, and MetS-associated factors

Variables	TSH	FT ₄	FT ₃
Age (years)	-0.007	-0.187	-0.151
BMI (kg/m ²)	0.121	0.127	0.570
WC (cm)	0.060*	-0.024	0.429
Fat ratio	0.084	0.091	0.351
SBP (mmHg)	-0.057	-0.083	-0.020
DBP (mmHg)	-0.078*	0.078	0.088
TC (mg/dl)	0.015**	-0.007*	0.128**
TG (mg/dl)	0.238	0.126*	0.218
HDL-C (mg/dl)	0.222	-0.156	0.141
LDL-C (mg/dl)	-0.029	-0.084*	0.129**
FBG (mg/dl)	0.008	0.091	0.273
Fasting insulin (μIU/ml)	0.023	0.189	0.238
HOMA-IR	0.018	0.187**	0.293

191 ** Correlation is significant at the *P*-values < 0.001 level (two-tailed)

192 * Correlation is significant at the *P*-values < 0.01 level (two-tailed)

193 NS

195 Discussion

196 MetS describes a constellation of different metabolic irregularities, which are often
197 associated with thyroid hormones and IR. The present study investigated the relationships

between thyroid hormones and IR in obese women diagnosed with MetS in Saudi Arabia. It is common knowledge that excessive weight gain and the resulting obesity increases the likelihood of incurring MetS. One of the risk factors for IR and hyperlipidemia is hypothyroidism. Hypothyroidism is associated with weight gain and concomitant changes to the other components that comprise MetS (Tarcin et al., 2012).

The present analysis established that HOMA-IR and TG values are comparatively higher in women that are MetS+ relative to their MetS- counterparts. Moreover, TSH was found to positively associate with WC and total cholesterol levels. The finding is in line with previous studies (Pergola et al., 2007, Ayturk et al., 2009). Increases in TSH concentration, weight, and TC level are likely indicative of subclinical hypothyroidism. This result serves as evidence for the association between elevated TSH levels and obesity and MetS. Correlations between hypothyroidism and IR have been thoroughly established by several earlier studies (Singh et al., 2010; Pergola et al., 2007; Ravi and Gokaldas, 2015). The analysis described here revealed positive associations between FT₄ and HOMA-IR values and fasting insulin levels. Low serum levels of free T₄ were observed in MetS+ women. This strongly suggests that low FT₄ levels mediate the development of IR. Thus, the association between thyroid hormone and HOMA-IR cannot be discounted and requires further investigation. In the present study, FT₄ and TG levels correlated positively, which is in contrast to one described a previous study (Kim et al., 2009). Furthermore, a positive correlation was observed between FT₄ and MetS-associated variables (Tarcin et al., 2012). Our results contradict the findings of Ayturk et al. (2009), who did not detect any correlation between free thyroid hormones and MetS. The increases in TC levels and LDL-C specifically are indicative of insulin sensitivity.

In the present study, increased FT₃ levels positively associated with increases in BMI. This is in accordance with a previous finding where associations between free or total thyroid hormone levels and body weight and BMI increases were observed (Roef et al., 2012). Interestingly, the increase in FT₃ concentration was independent of other metabolic parameters and insulin sensitivity; these results corroborate the findings of a previous study (Pergola et al., 2007). FT₃, alone or in combination with insulin, regulates the uptake and breakdown of glucose levels. A positive correlation between TG levels and HOMA-IR values was observed in MetS+ subgro

up in the present study. Some of the contradictory findings in the present study may stem from the study design or variations in the health status of the study subjects.

The HOMA approach is a reliable, time-tested method for quantifying IR that is both well established and regarded in the field. The HOMA-based analysis of MetS+ and MetS- obese women described here provides empirical evidence that BMI positively correlates with IR, which supports the findings of a previous, independent study (Geloneze et al., 2009). Moreover, the positive association between HOMA-IR values and elevated TG and total cholesterol levels nicely reflects its preponderance for MetS. Furthermore, the positive correlation between HOMA-IR values and TSH levels observed in the present study highlights the role played by the thyrotropin hormone in adipogenesis. These results are consistent with the findings of Bastemin et al. (2007) and were further validated using hierarchical clustering.

Declaration of interest

The author declares that that is no conflict of interest that may prejudice the impartiality of the present research.

References

- Ayturk S, Gursoy A, Kut A, Anil C, Nar A, Tutuncu NB. (2009). Metabolic syndrome and its components are associated with increased thyroid volume and nodule prevalence in a mild-to-moderate iodine-deficient area. *European Journal of Endocrinology*, 161, 599-605.
- Bastemir M, Akin F, Alkis E, Kaptanoglu B. (2007). Obesity is associated with increased serum TSH level, independent of thyroid function. *Swiss Medical Weekly*, 137, 431-4.
- Chakrabarti S, Guria S, Samanta I, Das M. (2007). Thyroid dysfunction modulates glucoregulatory mechanism in rat. *Indian Journal of experimental Biology*. 45, 549-553.
- Danaei G, Lu Y, Singh GM, Carnahan E, Stevens GA, Cowan MJ, Farzadfar F, Lin JK, Finucane MM, Rao M, Khang YH et al. (2014). Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardio metabolic risk factors from 1980 to 2010: a comparative risk assessment. *Lancet Diabetes and Endocrinology*, 2,634-47.
- Farasat T, Cheema AM, Khan MN. (2011). Relationship of thyroid hormones with serum fasting insulin and insulin resistance in euthyroid glycemic anomalies. *Pakistan Journal of Zoology*. 43, 379-386.
- Ferrannini E. (2004). Hyperinsulinemia and insulin resistance. In: *Diabetes: A fundamental and clinical text*, 3rd edn. (eds. D. Le Roith, S.I. Taylor and J.M. Olefsky).
- Ford ES. (2005). Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome. *Diabetes Care*, 28, 1769-78.
- Geloneze B, Vasques ACJ, Stabe CFC, Pareja JC, Rosado LEFPL, Queiroz ECD, Tambascia MA. (2009). HOMA1-IR and HOMA2-IR indexes in identifying insulin resistance and

metabolic syndrome-Brazilian metabolic syndrome study (BRAMS). *Arquivos Brasileiros de Endocrinologia & Metabologia*, 53, 281-287.

Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, McDermott MT. (2004). Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. *Endocrine Practice*, 10, 497–501.

Grundey SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa American Heart Association, F. & National Heart, Lung, and Blood Institute. (2005) Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 112, 2735–2752.

Harris MI, Flegal KM, Cowie CC, Eberhard MS, Goldstem DE, Little RR, Wiedmeyer HM, Byrd-Holt DD, (1998). Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The 3rd National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*, 4, 518-524.

Hoogwerf BJ, Nutall FQ. (1984). Long-term weight regulation in treated hyperthyroid and hypothyroid subjects. *American Journal of Medicine*, 76, 963–970.

Kim BJ, Kim TY, Koh JM, Kimt HK, Park JY, Lee KU, Shong YK, Kim WB. (2009). Relationship between serum free T4 (FT4) levels and metabolic syndrome (MS) and its components in healthy euthyroid subjects. *Clinical Endocrinology*, 70, 152-160.

Klieverik LP, Janssen SF, Van Riel A., Foppen E, Bisschop PH, Serlie MJ, Boelen A, Ackermans MT, Sauerwein HP, Fliers E, Kalsbeek A.(2009). Thyroid hormone modulates glucose production via a sympathetic pathway from the hypothalamic

paraventricular nucleus to the liver. Proceeding of National Academy of Sciences, 106, 5966-5971.

Knudsen N, Laur Berg P, Rasmussen LB, Bulow L, Ovesen L, Jorgensen T. (2005). Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population,” Journal of Clinical Endocrinology and Metabolism, 90, 4019–4024.

Lacobellis G, Ribaud MC, Zappaterreno A, Lannucci, CV, and Leonetti F. (2005.) Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. Clinical Endocrinology. 62, 487-491.

Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treaher DF, Turner RC. (1985). Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 28, 412-9.

Naslund E, Andersson I, Degerblad M, Kogner P, Kral JG, Rossner S, Hellstrom PM. (2000). Associations of leptin, insulin resistance and thyroid function with long-term weight loss in dieting obese men. Journal of internal Medicine, 248, 299-308.

Pergola GD, Ciampolillo A, Paolotti S, Trerotolit P, Giorgino R. (2007). Free triiodothyronine and thyroid-stimulating hormone are directly associated with waist circumference, independently of insulin resistance, metabolic parameters and blood pressure in overweight and obese women. Clinical Endocrinology, 67, 265-269.

Ravi BV, Gokaldas SR. (2015). A Study on Assessment of Thyroid Stimulating Hormone and Insulin Resistance in Women with Polycystic Ovarian Syndrome. International Journal of Science and Research, 4, 1683-1686.

- Roef G, Lapauw B, Goemaere S, Zmierzak HG, Toye K, Kaufman JM. (2012). Body composition and metabolic parameters are associated with variation in thyroid hormone levels among euthyroid young men. *European Journal of Endocrinology*, 16, 719-726.
- Singh BM, Goswami B, Mallika V. (2010). Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. *Indian Journal of Clinical Biochemistry*, 25(2), 141-145.
- Tarcin O, Abanonu GB, Yazici D, Tarcin O. (2012). Association of metabolic syndrome parameters with TT3 and FT3/FT4 ratio in obese Turkish population. *Metabolic Syndrome and Related Disorders*, 10(2), 137-142.
- Topsakal S, Yerlikaya E, Akin F, Kaptanoglu B, Erürker T. (2012). Relation with HOMA-IR and thyroid hormones in obese Turkish women with metabolic syndrome. *Eating and weight disorder*, 17, e57-61.

Figures legends

Figure 1. Flowchart schematic of study subject selection using the inclusion and exclusion criteria

Figure 2. Comparison of clinical and metabolic characteristics according to HOMA-IR. Insulin-sensitive (green, n = 21) and insulin-resistant (blue, n = 51) obese women. * $P < 0.05$, ** $P < 0.001$. BMI = body mass index, WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, FBG = fasting blood glucose, TSH = thyroid-stimulating hormone, FT₄ = free thyroxine, FT₃ = free triiodothyronine.

Figure 3. Hierarchical cluster analysis showing a significant correlation between HOMA-IR values and clinical and metabolic characteristics between both groups.

graphical abstract

HOMA-IR
■ Sensitive ■ Resistant

Comparison of clinical and metabolic characteristics according to

Flowchart showing study subjects with inclusion and exclusion criteria

Fig.3 Shows a significant correlation among clinical a

Table 1. Anthropometric and biochemical variables in the study subjects (data are given as mean and standard deviation)

Variables	MetS+ (n=72)	MetS- (n=28)	P-value
Age (years)	33.12±9.06	28.64±8.39	NS
Body mass index (kg/m ²)	32.12±4.89	29.41±5.98	<0.05
Waist circumference (cm)	89.38±7.93	80.44±2.34	NS
Fat ratio	39.24±6.60	24.62±4.35	NS
Systolic blood pressure (mmHg)	132.12±9.48	112.10±10.91	<0.001
Diastolic blood pressure (mmHg)	88.34±8.43	78.78±4.31	NS
Total cholesterol (mg/dl)	234.67±9.79	193.94±9.75	<0.001
Triglyceride (mg/dl)	167.83±8.90	151.41±8.26	<0.001
HDL-C (mg/dl)	34.27±7.08	58.21±4.33	<0.05
LDL-C (mg/dl)	130.42±11.37	125.72±11.45	NS
Fasting blood glucose (mg/dl)	109.55±10.47	94.70±8.12	<0.001
TSH (mIU/l)	2.38±1.52	1.38±1.02	<0.05
FT ₄ (pmol/l)	11.96±2.81	10.56±2.46	NS
FT ₃ (pmol/l)	6.22±1.70	5.47±2.47	NS
Fasting Insulin (μIU/ml)	12.42±5.09	5.10±1.42	<0.05
HOMA-IR	5.14±2.13	1.61±1.02	NS

bioRxiv preprint doi: <https://doi.org/10.1101/595884>; this version posted April 1, 2019. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY 4.0 International license.

Table 2. Pearson correlation coefficients (r) of TSH, FT₄ and FT₃ with general, anthropometric and components of metabolic syndrome

Variables	TSH	FT ₄	FT ₃
Age (years)	-0.007	-0.187	-0.151
Body mass index (kg/m ²)	0.121	0.127	0.570
Waist circumference (cm)	0.060*	-0.024	0.429
Fat ratio	0.084	0.091	0.351
Systolic blood pressure (mmHg)	-0.057	-0.083	-0.020
Diastolic blood pressure (mmHg)	-0.078*	0.078	0.088
Total cholesterol (mg/dl)	0.015**	-0.007*	0.128**
Triglyceride (mg/dl)	0.238	0.126*	0.218
HDL-C (mg/dl)	0.222	-0.156	0.141
LDL-C (mg/dl)	-0.029	-0.084*	0.129**
Fasting blood glucose (mg/dl)	0.008	0.091	0.273
Fasting Insulin (μIU/ml)	0.023	0.189	0.238
HOMA-IR	0.018	0.187**	0.293

** Correlation is significant at the 0.001 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).