

Association of Visceral adiposity Index (VAI) with Glycemic control in Metabolic Syndrome (MetS)

Dr. Remal Abdulaziz Asaad*

(Received 3 / 8 / 2022. Accepted 2 / 10 / 2022)

□ ABSTRACT □

Background: Visceral Adiposity Index (VAI) is suggested as an effective adipose tissue marker that reflects the visceral obesity and the degree of visceral lipid distribution. Metabolic Syndrome (MetS) is one of the most common metabolic abnormalities in Type II Diabetes Mellitus (T2DM). **Objective:** to evaluate the prevalence of MetS in T2DM, and the association of VAI with glycated hemoglobin (HbA1C) as a marker of glycemic control. The current study was conducted in 129 T2DM (62 males and 67 females) at Tishreen University Hospital and Diabetes Center of Lattakia-Syria between 2020 and 2021. **Results:** 90 patients (69.77%) were diagnosed with MetS. VAI index increased with the severity of MetS as compared to the body mass index (BMI) and waist circumference (WC) as global obesity markers. VAI increased with HbA1C levels $\geq 8\%$, ($p=0.003$). Using receiver operating characteristic (ROC) curve, the best cutoff point for VAI to predict poor glycemic control was (1.9), with a sensitivity of (70%) and a specificity of (51%). Area under the curve (AUC) of VAI was the largest compared with WC or BMI. **Conclusion:** Strong association between VAI as a marker of visceral adipose tissue and elevated HbA1C levels as poor glycemic control marker in MetS.

Keywords: Visceral adiposity Index (VAI), Glycated Hemoglobin (HbA1C), Metabolic Syndrome (MetS), Type II Diabetes Mellitus (T2DM).

*Assistant professor in Biochemistry and Microbiology department- Faculty of Pharmacy-Tishreen University- Lattakia-Syria.

العلاقة بين مشعر البدانة الحشوية (VAI) والضبط الغلوكوزي لدى مرضى المتلازمة الاستقلابية

د. رمال عبد العزيز أسعد*

(تاريخ الإيداع 3 / 8 / 2022. قُبِلَ للنشر في 2 / 10 / 2022)

□ ملخص □

تعد المتلازمة الاستقلابية من أشيع الاضطرابات الاستقلابية لدى مرضى الداء السكري النمط الثاني. الهدف: هدف البحث لتقييم معدلات انتشار المتلازمة الاستقلابية لدى مرضى الداء السكري النمط الثاني، وكذلك دراسة العلاقة بين VAI ومستويات الخضاب الغلوكوزي كمشعر لدرجة ضبط الغلوكوز. شملت الدراسة 129 مريض داء سكري نمط ثاني (62 ذكر و67 أنثى) من المراجعين لمركز السكري ومشفى تشرين الجامعي في مدينة اللاذقية-سوريا. جمعت العينات بين عامي 2020 و2021. النتائج: أظهرت النتائج إصابة 90 مريض داء سكري بالمتلازمة الاستقلابية (69.77%). ارتفاع مستويات VAI مع زيادة شدة المتلازمة الاستقلابية بالمقارنة مع مشعر كتلة الجسم BMI ومحيط الخصر WC كمشعرات للبدانة الكلية. ترافق ارتفاع VAI مع ارتفاع مستويات الخضاب الغلوكوزي $\leq 8\%$ ويشكل هام احصائيا ($p=0.003$). بلغت القيمة الحدية لمشعر VAI: 1.9، بحساسية 70% ونوعية 51% حيث كانت AUC هي الأكبر مقارنة مع BMI والـ WC. الخاتمة: أظهرت نتائج البحث ارتباطاً وثيقاً بين ارتفاع مستويات VAI كواسم للبدانة الحشوية والمستويات المرتفعة من الخضاب الغلوكوزي HbA1C كمشعر للضبط الغلوكوزي السيئ لدى مرضى المتلازمة الاستقلابية.

الكلمات المفتاحية: مشعر البدانة الحشوية VAI، الخضاب الغلوكوزي HbA1C - المتلازمة الاستقلابية MetS - الداء السكري النمط الثاني T2DM

* أستاذ مساعد - قسم الكيمياء الحيوية والأحياء الدقيقة - كلية الصيدلة - جامعة تشرين - اللاذقية - سورية

Introduction:

adipose tissue dysfunction is one of the proposed mechanisms for systemic metabolic complications, such as low grade inflammation, insulin resistance (IR), dyslipidemia and dysglycemia [1]. It has been associated with an increased incidence of obesity (particularly central obesity) and Metabolic Syndrome (MetS) in the population and has been described as a morbidity and mortality risk factor in both normal weight and obese subjects ([2].

MetS with notable incidence worldwide (it varies from 8% to 43% in men and from 7% to 56% in women) is a complex of interrelated and heterogeneous risk factors for cardiovascular and coronary heart diseases in Type II Diabetes Mellitus (T2DM) [2]. MetS is characterized and diagnosed with dysglycemia, raised blood pressure, dyslipidemia, and obesity, according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III). In 2009 criteria proposed by (NCEP-ATPIII) was modified with respect to waist circumference (WC) as a central obesity marker, which varies in different populations as well as in Asian population [3, 4].

Visceral fat is strongly correlated with metabolic abnormalities, IR and cardiovascular disease than subcutaneous fat or overall obesity. In fact, visceral adipose tissue provides a microenvironment of low grade- inflammatory; with a higher rate of lipolysis (increased serum free fatty acids and Triglyceride (TG)), pro-inflammatory cytokines' secretion such as Interleukin-6, Tumor Necrosis Factor (TNF), and decreased level of Adiponectin hormone due to increased levels of Resistin hormone [5]. Therefore; inactivation of insulin signaling pathway in adipose tissue associated with dysglycemia and dyslipidemia have been investigated in T2DM patients [6].

Assessing of adipose tissue dysfunction using overall obesity markers such as WC and Body Mass Index (BMI) cannot distinguish visceral from subcutaneous fat; they cannot effectively differ between the fat and muscle. Magnetic resonance imaging (MRI) and Computerized tomography scan (CT) can quantify visceral fat tissue and distinguish between various types of body fat distribution, especially subcutaneous and visceral fat tissue, but these procedures are expensive and not available in every clinical setting [7]. Therefore, there is a need for simple alternatives and less expensive markers of adipose tissue that can quantify visceral fat.

Recently, Visceral Adiposity Index (VAI) is suggested as a surrogate marker of visceral adiposity based on metabolic parameters: Triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and anthropometric parameters (BMI and WC) in men and women. VAI that reflects the degree of fat distribution and accumulation of visceral lipid is a better important and more effective adipose tissue index compared to WC and BMI that reflect the overall obesity [8, 9]. A strong relationship between the use of VAI and hyperglycemia, IR in T2DM has been determined in many researches. Furthermore, there is evidence that increased WC is associated with the aggravation of TG levels as well as a notable association between TG level and risk of metabolic syndrome in T2DM patients [10]. Therefore; the evaluation of abdominal fat, as a risk factor for poor glycemic control associated with MetS, is more efficient by estimating the VAI using a simple formula based on metabolic parameters (TG, HDL-C) and markers of overall obesity (WC, BMI) [11].

Aims of the current study were to evaluate the prevalence of Metabolic Syndrome (MetS) in type II Diabetes Mellitus (T2DM), and the association between Visceral Adiposity Index (VAI) and Glycemic control (using HbA1C) in patients diagnosed with MetS.

Methods and Materials:

From November 2020 to December 2021, one hundred twenty-nine T2DM patients (62 males and 67 females) were initially enrolled in this study which took place at Tishreen University Hospital (TUH) and Diabetes Center of Lattakia City, Syria. Demographic data and clinical information of participants were collected using a standardized questionnaire after an informed written consent was collected from all participants.

Study population:

Inclusion criteria: T2DM patients aged from 25 to 83 years, on oral hypoglycemic drugs were included in the study. Mean duration of disease was 5.52 ± 3.89 years.

Exclusion criteria: subjects with type 1 diabetes, presenting with a history of major medical illness such as, cancer, thyroid and endocrine dysfunction, and women with polycystic ovary syndrome (PCOS) were also excluded.

Anthropometric measurements: weight (kg) and height (m) were measured with light clothes, barefoot.

1) **Body Mass Index (BMI)** was calculated based on weight (kg)/height² (m). Participants were divided as following according to the World Health Organization (WHO) classification:

- Normal weight with $BMI < 25 \text{ kg/m}^2$
- Over weight with $BMI: 25- 29.9 \text{ kg/m}^2$
- Obesity with $BMI \geq 30 \text{ kg/m}^2$

2) **Waist Circumference (WC)** in cm: was obtained from all participants standing in both feet and both arms hanging freely, using a plastic, flexible, inelastic measuring tape in the middle point between the lower costal rib and the iliac crest in a perpendicular plane.

The abdominal obesity thresholds were defined according to the World Health Organization criteria ($WC > 88$ cm, for women, $WC > 102$ cm, for men).

Systolic and diastolic blood pressures (**SBP/DBP**) were measured twice using mercury sphygmomanometer and the readings were averaged.

Visceral Adiposity Index (VAI): VAI calculation was performed using the gender-specific equations proposed by Amato et al. [11]:

- a. VAI (male): $(WC / [39.68 + (1.88 * BMI)]) \times (TG / 1.03 * 1.31 / HDL-C)$ (mmol/l).
- b. VAI (female): $(WC / [36.85 + (1.89 * BMI)]) \times (TG / 0.81 * 1.52 / HDL-C)$ (mmol/l).

Biochemical measurements:

Under aseptic precautions, overnight fasting blood samples from T2DM participants were taken into two tubes:

a - Plain vacutainer tube: sample was centrifuged at 1500 rpm for 10 min at 25°C and the separated serum was used for the following biochemical tests: fasting blood glucose (FBG), HDL-C, and TG.

b - Tube containing dipotassium Ethylenedinitro tetra acetic (EDTA) anticoagulant: the whole blood sample was used for the test of Glycated Hemoglobin (HbA1C).

Patients were considered dyslipidemic when serum TG levels ≥ 150 mg/dl, and with serum HDL-C levels ≤ 40 mg/dl for male, and ≤ 50 mg/dl for female.

MetS was diagnostic according to (NCEP-ATPIII) criteria with the presence of 3 of the following:

1. Systolic blood pressure of ≥ 130 mmHg, diastolic blood pressure of ≥ 85 mmHg, or treatment of diagnosed systemic hypertension.
2. $FBG \geq 110$ mg/dl or previously diagnosed T2DM.
3. $HDL-C < 40$ mg/dl in male and < 50 mg/dl in female.

4. TG \geq 150 mg/dl or specific treatment for elevated TG.
5. WC >88 cm in women, and >102 cm in men.

T2DM patients with MetS (MetS+) were divided into three subgroups with increasing severity of MetS according to the number of criteria; **MetS-3, MetS-4, MetS-5.**

Analytical Measurements and Instrumentation:

FBG was tested by HumaLyzer Primus; Semi Automatic Microprocessor Controlled Photometer/Germany, HDL-C and TG were measured by Mindary BS-380 clinical chemistry analyzer/China. All biochemical investigations were performed according to the manufacturer’s protocol using commercially available Kits from Biosystem®, Spain.

HbA1C was measured using the technique of High-Performance Liquid Chromatography (HPLC) by Tosoh Automated Glycohemoglobin Analyzer (HLC®-723GX)/India.

Statistical analysis: Results were analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for windows. Data were presented as mean± standard deviation (SD). Student's t-test was used to compare the means of different variables between two independent samples. Analysis of variance (ANOVA) of one factor was used to identify differences among means. Person's coefficient was performed to show the linear correlation between different variables. Results were expressed as a p.value; results with p.value \leq 0.05 was considered statistically significant.

Results:

The current study was performed in (129) T2DM patients, 62 males (48%) and 67 females (52%), with mean age (46.63±11.35 years), and mean disease duration (5.52±3.89 years). The mean levels of FBG and HbA1C were (146.37±56.34 mg/dl) and (8.25±1.68 %) respectively. Regarding obesity markers; the patients had a mean BMI (29.05±4.42 kg/cm²), and a mean WC of (108.13±17.59 cm) for males and (112.23±12.03 cm) for females. (Table 1) shows baseline characteristics, serum TG and HDL-C levels of T2DM patients.

| parameter | T2DM (Mean± SD) | n, % |
|--------------------------------------|---|---|
| Age (Years) | 46.63±11.35 | |
| Sex | | |
| Male | - | 62, (48%) |
| Female | | 67, (52%) |
| FBG (mg/dl) | 146.37±56.34 | <150: 70, (54.26%) ≥150: 59, (45.745%) |
| HbA1C (%) | 8.25±1.68 | <8: 60, (46.51%) ≥ 8: 69, (53.49%) |
| Duration of disease (years) | 5.52±3.89 | - |
| Body Mass Index (kg/m ²) | 29.05±4.42 | <25: 25, (19.38%) ≥25: 104, (80.62%) |
| Waist Circumference (Cm) | Male:108.13 ± 17.59 Femeale:112.23±12.03 | 62, (48%) 67, (52%) |
| SBD* (mmHg) | 119.72 ±9.52 | |
| DBP*(mmHg) | 83.81±7.79 | - |
| Triglycerides TG (mg/dl) | 171.13±58.60 | < 150: 33, (25.58%) ≥150: 96, (74.42%) |
| HDL-Cholesterol (mg/dl) | 57.62±15.05 | Males: < 40: 37, ≥ 40: 25 Females: <50: 30, ≥ 50: 37 |

Table2: distribution of MetS patients according to obesity markers (WC, BMI and VAI), TG, HDL-C and HbA1C

| Parameter | MetS(n=90) | | |
|--------------------------|--------------|-------------|--------------|
| | Mean± SD | Lower Value | Higher Value |
| Age (years) | 57±9.11 | 27 | 83 |
| VAI | 2.45±0.69 | 0.69 | 8.40 |
| WC (cm) | 105.57±12.65 | 78 | 150 |
| BMI (kg/m ²) | 29.11±4.42 | 21.32 | 44.78 |
| HbA1C (%) | 8.54±2.24 | 5.5 | 15.4 |
| HDL-C (mg/dl) | 51.34±13.43 | 31 | 105 |
| TG (mg/dl) | 147.36±51.87 | 68 | 321 |

*SBD: systolic blood pressure , DBP: diastolic blood pressure

(Table 2) shows the distribution of MetS patients according to obesity markers (WC, BMI and VAI), TG, HDL-C and HbA1C.

Among 129 T2DM, 90 patients were diagnosed with MetS (69.77%) according to (NCEP-ATPIII) criteria. MetS Patients aged from 27 to 83 years with mean age of (57±9.11 years), and their HbA1C ranged from 5.5% to 15.4%, with mean of (8.54±2.24%) representing a poor glycemic control. Mean BMI and WC in MetS

patients were (29.11±4.42kg/m², and 105.57±12.65cm respectively) pointing to overweight population. VAI ranged from 0.69 to 8.40 with mean of (2.45 ±0.69). Concerning the lipid profile; serum HDL-C ranged from (32 to 105 mg/dl), while serum TG range from (68 to 321mg/dl) with notable lipid abnormalities.

(Table 3) shows the results concerning VAI, BMI and WC as obesity markers in MetS groups according to increased number of MetS criteria. Results confirm the association between increased VAI values and severity of MetS with significant difference between the three groups (p=0.001) . BMI and WC do not seem to be related to MetS severity (p>0.05).

Table3: Visceral adiposity Index VAI, BMI and WC markers in patients with MetS according to number of MetS criteria

| Parameters | N= 90, (69.77%) | | | P.value |
|-------------------------------|-----------------|----------------|----------------|---------|
| | MetS-3 | MetS-4 | MetS-5 | |
| | n=34, (37.77%) | n=44, (48.88%) | n=12, (13.33%) | |
| Male | 20 | 17 | 6 | |
| Female | 14 | 27 | 6 | |
| BMI Mean ±SD:(28.80±4.42) | 28.48±3.8 | 29.06±3.8 | 31.07±7.11 | 0.221 |
| WC Mean± SD:(105.57±12.65) | 102.91±11.40 | 106.72±13.92 | 108.91±10.41 | 0.261 |
| VAI Mean ± SD: (2.46±1.36) | 1.81±0.62 | 2.7±1.57 | 3.19±1.38 | 0.001 |

| Parameter | | N | VAI Mean \pm SD | <i>P.value</i> | r | <i>p.value</i> |
|---------------------|----------|----|----------------------|----------------|-------|----------------|
| HbA1C | <8 | 49 | 2.07 \pm 1.01 | 0.003 | 0.211 | 0.046 |
| | \geq 8 | 41 | 2.91 \pm 1.57 | | | |
| FBG | <110 | 10 | 2.01 \pm 0.1 | 0.04 | 0.301 | 0.03 |
| | 110-150 | 38 | 2.12 \pm 1.1 | | | |
| | >150 | 42 | 2.6 \pm 1.03 | | | |
| Duration of disease | <5 | 29 | 2.32 \pm 1.2 | 0.531 | 0.06 | 0.531 |
| | \geq 5 | 61 | 2.5 \pm 1.41 | | | |
| sex | Male | 43 | 2.03 \pm 1.1 | 0.004 | - | - |
| | Female | 47 | 2.84 \pm 1.40 | | | |

(Table 4) represents the results of the association between VAI and Glycemic control in MetS patients. The data showed that elevated HbA1C values were associated with significant increase in the average of VAI ($P=0.003$). In addition, the Pearson's test showed a significant positive correlation between HbA1C and VAI index ($r=0.211$, $P<0.05$). Patients with T2DM ≥ 5 years had an increase in VAI compared to the other group but the difference was not significant. The Pearson's test also showed no correlation between disease duration and VAI ($P>0.05$). Elevated FBG levels were associated with a significant increase in the mean of VAI ($P<0.05$). Females had a significant increase in the mean of VAI compared to males ($p=0.004$). Regarding the relationship of BMI and WC with Glycemic control; data showed that elevated HbA1C or FBG were not associated with increase BMI or WC ($P>0.05$). In addition, there was no relationship of sex with increased BMI, or WC (data not shown).

(Table 5) and (figure 1) represent the results of Receiver Operating Characteristic Curves (ROC) of VAI, WC, And BMI for prediction of poor Glycemic Control ($\geq 8\%$) in MetS patients. The largest AUC was with VAI (0.696) with cutoff of 1.9, sensitivity: (70%) and specificity: (51%) compared to BMI and WC, which showed AUC of 0.418 and 0.488 respectively. Cutoff values of BMI and WC for predicting poor glycemic control in MetS were (27.55 kg/m²) and (120.5 cm) respectively, with poor sensitivity and specificity.

| Parameter | AUC | Cut-off value | Sensitivity % | Specificity % |
|-----------|-------|---------------|---------------|---------------|
| VAI | 0.696 | 1.9 | 70% | 51% |
| BMI | 0.418 | 27.55 | 58% | 33% |
| WC | 0.488 | 102.5 | 58% | 37% |

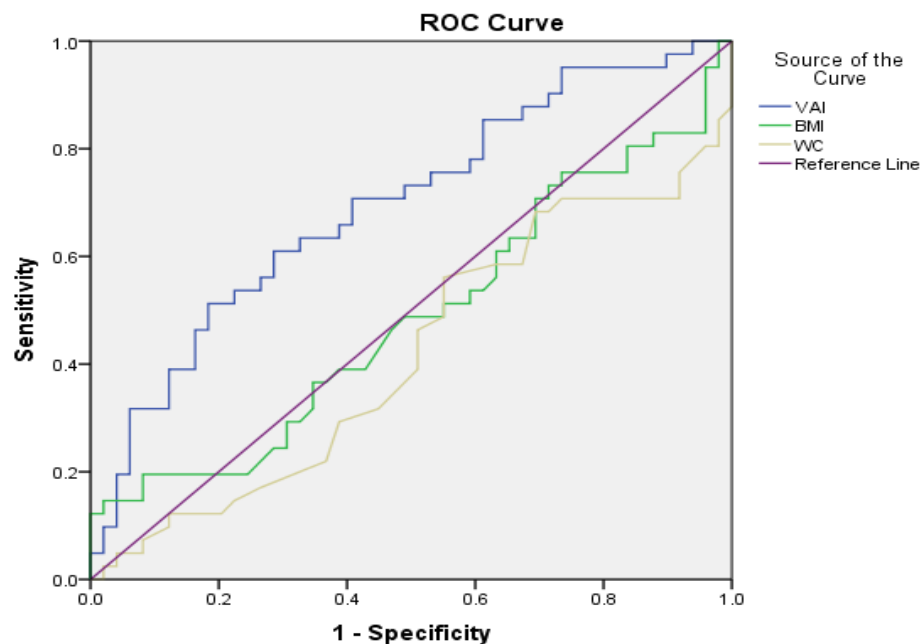


Figure1: ROC curves of VAI, WC, and BMI for prediction of poor glycemic control ($\geq 8\%$) in Mets patients. AUC of VAI was the largest in comparison with AUC of BMI and WC. VAI: Visceral Adiposity Index, BMI: Body Mass Index, WC: Waist Circumference.

Discussion:

For most obese individuals, the risk of developing metabolic syndrome (MetS) is evident; central obesity has been strongly associated with severe abnormalities in the metabolic profile compared to general obesity. Moreover, with the increasing incidence of obesity and adipose tissue abnormalities worldwide, their association with poor glycemic control in T2DM has been widely studied and confirmed. Due to the requirement for highly sophisticated techniques to assess visceral adiposity, there was an urgent need to find new easily performed markers such as the Visceral Adiposity Index VAI. [12].VAI represents a new, simple and non-expensive marker for estimation of visceral fat in comparison with overall obesity markers (BMI, WC) that cannot distinguish fat from muscle. Various factors that influence the glycemic control have been widely studied [13,14]. So, we aimed in this study to estimate the incidence of MetS in T2DM, and the predictive value of VAI for poor glycemic control in MetS among T2DM patients.

The present study was conducted on 129 T2DM aged 27 - 83 years, and with a mean disease duration of (5.52 ± 3.89 years) at Tishreen University Hospital (TUH) and the Diabetes Center of Lattakia, Syria.

Our results show that 90 patients were diagnosed with MetS among T2DM according to (NCEP-ATP-III) with the presence of three criteria (explained previously) and with notable incidence of (69.77%). The results of (Gelfand, J.M, et al, 2005) showed incidence of (62%), which confirms a rising prevalence of MetS worldwide, and a notable prevalence in developing countries probably due to lifestyle, obesity, and the increased prevalence of T2DM [15]. Recently, it has been shown that patients with MetS have a 3.5-fold higher risk to develop an atheroma plaque. Thus, MetS identifies a group of high-risk individuals who would have been overlooked by considering only the conventional risk factors. Therefore; dysfunction of adipose tissue and abdominal obesity markers, such as VAI have

been widely studied. Our results showed that VAI was more effective in identifying the severity of MetS (as assessed by an increased number of MetS criteria) with a statistically significant difference (p -value= 0.001) than BMI and WC. BMI is a scale of overweight and obesity, but should be used conservatively in epidemiological studies to estimate the risk caused by the over accumulation of body fat [16]. Kishida et al., in 2012 confirm that over accumulation of body fat in the viscera represents an additional health risk, but BMI does not imply any thorough understanding of partial body fat distribution and accumulation [16,17].

To better understand the influence of VAI as a visceral marker on patients with MetS as high-risk individuals, we investigated the relation of VAI with dysglycemia. The results shown in table 4 confirm the association between VAI and poor glycemic control; HbA1C levels were higher ($\geq 8\%$) in patients with increased VAI values, and the difference was statistically significant (p -value=0.003) compared to BMI and WC. Liu et al. in 2016, showed that elevated VAI levels are positively associated with the presence of pre-diabetes and diabetes in Chinese adults [18]. In addition, VAI was significant with sex; females had higher VAI levels than BMI or WC, and this correlates with the results of Hameed, et al, in 2019 [19].

The relation between visceral adiposity and poor glycemic control in MetS patients can be explained by the excessive release of free fatty acids (FFAs) from the visceral adipose tissue, with higher rates of lipolysis than subcutaneous fat [12]. In addition, visceral adipose tissue lipolysis show high insulin resistance (IR), and high activity of Hormone Sensitive lipase (HSL) leading to increased supply of free fatty acid to the liver by the portal reused of FFAs [17]. HbA1c level would be 0.8% higher for each 50-cm increase in the visceral fat [19].

To identify the cutoff values of BMI, WC and VAI that predict the poor glycemic control, Receiver Operating Characteristic Curve (ROC) Analysis, Sensitivity and Specificity were studied. Results shown in (table 5 and figure 1) confirm that VAI was the best obesity marker in comparison with BMI and WC to predict a bad glycemic control in MetS; the cutoff value of VAI was (1, 9) with a sensitivity of (70%), specificity of (51%), and AUC of (0.696). This means that patients having MetS and $VAI \geq 1.9$ will be with HbA1C level ($\geq 8\%$) as uncontrolled T2DM patients. These patients need a better management protocol including: a strict diet, a healthy lifestyle, drugs against hyperglycemia and other procedures that may reduce HbA1C%.

Conclusion:

Notable incidence of obesity and MetS was observed in T2DM patients among Syrian-population. Increased VAI was associated with the severity of MetS, and strongly affects HbA1C levels in T2DM with MetS compared to BMI and WC.

Visceral tissue abnormality exhibits a pattern of dysglycemia and dyslipidemia, and this suggests the beneficial measurement of the visceral fat markers as part of the clinical phenotyping and management strategy in T2DM.

For most obese individuals, the risk of developing metabolic syndrome (MetS) is evident; central obesity has been strongly associated with severe abnormalities in the metabolic profile compared to general obesity. Moreover, with the increased incidence of obesity and adipose tissue abnormalities worldwide, which is strongly associated with poor glycemic control among T2DM; there is a need for evaluation of visceral fat using new markers such as Visceral Adipose Index VAI [12]. Therefore, VAI presents a new, simple and non-expensive marker for estimation of visceral fat in comparison with overall obesity markers (BMI, WC) that cannot distinguish fat from muscle. Various factors that influence the

glycemic control have been widely studied [13,14]. So, we aimed in this study to estimate the incidence of MetS in T2DM, and the predictive value of VAI for poor glycemic control in MetS among T2DM patients.

Our results show that 90 patients were diagnosed with MetS among T2DM according to (NCEP-ATP-III) with the presence of three criteria (explained previously) and with notable prevalence of (69.77%). The results of (Gelfand, J.M, et al, 2005) showed incidence of (62%), which confirms a rising prevalence of MetS worldwide, and notable prevalence in developing countries due probably to lifestyle, obesity, aging of population and increased prevalence of T2DM [15]. Recently, it has shown that patients with MetS have a 3.5-fold higher risk of the presence of an atheroma plaque. Therefore, MetS identifies high-risk group of individual who would have been missed by considering only the conventional risk factors. Thus; dysfunction of adipose tissue and abdominal obesity markers, such as VAI have been widely studied. Our results showed that VAI was more effective to identify the severity of MetS according to increased number of MetS criteria with statistically significant difference ($p.value= 0.001$) in comparison with BMI and WC as overall obesity markers. In addition, BMI is a scale of overweight and obesity, but should be used conservatively in epidemiological studies to estimate the risk caused by the over accumulation of body fat [16]. Kishida et al., in 2012 confirmed that over accumulation of body fat in the viscera presents an additional health risk, but BMI does not imply any thorough understanding of partial body fat distribution and accumulation [16, 17].

For more understanding the influence of VAI as a visceral marker on patients with MetS as high risk individuals, we studied the relation of VAI with dysglycemia. Results shown in table 4 confirm the association between VAI and poor glycemic control; HbA1C levels were higher ($\geq 8\%$) in patients with increased VAI values, and the difference was statistically significant ($p.value=0.003$) compared with BMI and WC. Liu et al. in 2016, confirmed that elevated VAI level are positively associated with the presence of pre-diabetes and diabetes in Chinese adults [18]. In addition, VAI was significantly related to sex; females were with higher VAI levels compared with BMI or WC, and this correlates with the results obtained by Hameed, et al, in 2019 [19]. The relationship between visceral adiposity and poor glycemic control in MetS patients can be explained by the excessive release of free fatty acids (FFAs) from the visceral adipose tissue, with higher rates of lipolysis than subcutaneous fat [12]. In addition, visceral adipose tissue lipolysis shows high resistance rate for insulin (IR), and high activity of Hormone Sensitive lipase (HSL) lead to increased delivery of free fatty acid to the liver by the portal reused of FFAs [17]. HbA1c level would be 0.8% higher for each 50-cm increase in the visceral fat [19].

To identify the cutoff values of BMI, WC and VAI that predict the poor glycemic, Receiver Operating Characteristic Curve (ROC) analysis, sensitivity and specificity were studied. Results shown in (table 5 and figure 1) confirm that VAI was the best obesity marker in comparison with BMI and WC to predict the poor glycemic in MetS; cutoff value of VAI was (1, 9). Patients with MetS with VAI=1.9 or more will be with HbA1C level ($\geq 8\%$) as uncontrolled T2DM patients with a sensitivity of (70%), and specificity of (51%), while BMI and WC were ineffective to predict the poor glycemic. This suggests the need of better management protocol in patients including: diet, lifestyle, hypo-glycemia drugs and other procedures that reduce HbA1C%.

Conclusion:

Notable prevalence of obesity and MetS in T2DM patients in study population as a part of Syrian-patients. Increased VAI associates with the severity of MetS, and strongly affects the HbA1C levels in MetS with T2DM compared with BMI and WC.

Visceral tissue presents dysglycemia and dyslipidemia profile, and this suggests the beneficial measurement of the visceral fat markers as part of clinical phenotyping and management strategy in T2DM.

References:

1. HAJER, G.R.; VISSEREN, F.L. *Adipose tissue dysfunction in obesity, diabetes, and vascular diseases*, Eur. Heart J. 29, 2008, 2959-2971.
2. KRANENDORK, M.E.; HAEFTEN, T.W.; STUPKOVA, T.; JAGER, W.; VINK, A. et al., *Inflammatory characteristics of distinct abdominal adipose tissue depots relate differently to metabolic risk factors for cardiovascular disease: distinct fat depots and vascular risk factors*, Atherosclerosis. 239, 2015, 419-427.
3. ARIMURA, S.T.; MOURA, B.M.; PIMENTAL, G.D.; et al. *Waist circumference is better associated with high density lipoprotein (HDL-c) than with body mass index (BMI) in adults with metabolic syndrome*, Nutr Hosp. 2011, 26, 1328-1332.
4. ALBERTI, K.G.; ECKEL, R.H.; GRUNDY, S.M., et al. *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; and International Association for the Study of Obesity*. Circulation. 2009, 120, 1640-1645.
5. KONDO, T.; KISHI, M.; FUSHIMI, T.; UGAJIN, S.; KAGA, S. *Vinegar intake reduces body weight, body fat mass, and serum triglyceride levels in obese Japanese subjects*, Bioscience, Biotechnology, and Biochemistry. 2009, 73, 1837-1843.
6. KISHIDA, K.; FUNAHASHI, T.; MATSUZAWA, Y.; SHIMOMURA, I. *Visceral adiposity as a target for the management of the metabolic syndrome*, Annals of Medicine. 2012, 44(3), 233-241.
7. HASLAM, D.W.; JAMES, W.P. *Obesity*, Lancet. 2005, 366, 1197-1209.
8. TAIAN, T.; PEI, H.; CHEN, Z.; HAILILI, G.; WANG, S.; SUN, Y.; YAO, H.; JIANGHONG, D. *Comparison of lipid accumulation product and body mass index as indicators of diabetes diagnosis among 215,651 Chinese adults*, PeerJ. 2020, 8:e8483 DOI 10.7717/peerj.8483.
9. ANOOP, S.; DASGUPTA, R.; REBEKAH, G. *product (LAP) as a potential index to predict risk of insulin resistance in young, non-obese Asian Indian males from hyperinsulinemic-euglycemic clamp studies*, BMJ Open Diab Res Care. 2021, 9, 1110-1136/bmjdr-002414.
10. MOTAMED, N.; RAZMJOU, S.; HEMMASI, G.; MAADI, M.; ZAMANI, F. *Lipid accumulation product and metabolic syndrome: a population-based study in northern Iran*, Amol, Journal of Endocrinological Investigation. 2016, 39(4), 375-382.
11. AMATO, M. C.; GIORDANO, C.; GALIA, M. et al., *Visceral adiposity index: a reliable indicator of visceral fat function associated with cardiometabolic risk*, Diabetes Care. 2010, 33, 920-922.
12. CAO, Y.Y.; TANG, X.; SUN, K.X.; LIU, Z.K.; XIANG, X.; JUAN, J.; et al. *Relationship between glycemic control and visceral adiposity index among the patients with type 2 diabetes mellitus*, Beijing. Da Xue Xue Bao Yi Xue Ban. 2017, 49(3), 446-450.

13. ASAAD, R.; KHAIAT, M.; BARAKAT, K. *Evaluation of plasma Magnesium Levels and its Correlation with Glycemic Control in Type 2 Diabetes Mellitus Patient*, Tishreen University Journal-Medical Sciences Series.2018, 39(2).
14. AL-MERI, M.; HAMDAN, R.; SAABOUH, A. *the relationship between serum magnesium and type 2 diabetes mellitus*, Tishreen University Journal-Medical Sciences Series. 2021, 43(4).
15. GELFAND, J.M.; WEINSTEIN, R.; PORTER, S.B.; et al. *Prevalence and treatment of psoriasis in the United Kingdom: A populationbased study*, Arch Dermatol. 2005, 141, 1537–1541.
16. KISHIDA, K.; FUNAHASHI, T.; MATSUZAW, Y.; SHIMOMUR, I. *Visceral adiposity as a target for the management of the metabolic syndrome*, Annals of Medicine. 2012, 44(3):233–241.
17. DESPRES, J-P. *Is visceral obesity the cause of the metabolic syndrome?* Annals of Medicine, 2006. 38(1):52–63.
18. LIU, P.; MA,F.; LOU, H.; CHEN, Y. *Visceral adiposity index is associated with prediabetes and type 2 diabetes mellitus in Chinese adults aged 20-50*, Ann Nutr Metab. 2016, 68, 243-253.
19. HAMEED, E. K.; ABDULQAHAR, Z.H. *Visceral adiposity index in female with type 2 diabetic mellitus and its association with the glycemic control*, Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019, 13, 1241-1244.