Research Paper

Insulin resistance in Saudi postmenopausal women with and without metabolic syndrome and its association with vitamin D deficiency

Eman M. Alissa, PhD a,*, Wafa A. Alnahdi, MSc a, Nabil Alama, PhD a, Gordon A. Ferns, MRCS, FRCPath b

a Faculty of Medicine, King Abdulaziz University, PO. Box 12713, Jeddah 21483, Saudi Arabia
b Medical Education and Metabolic Medicine, Brighton and Sussex Medical School, University of Brighton, BN1 9PH, UK

Abstract

Background: There is increasing interest in the non-skeletal effects of vitamin D and the relationship between vitamin D deficiency and chronic conditions such as diabetes mellitus. We aimed to investigate the relationship between surrogate indices of insulin resistance (IR), and vitamin D deficiency/insufficiency in postmenopausal Saudi women with and without metabolic syndrome.

Methods: The study population consisted of 300 postmenopausal women aged 46–88 years enrolled consecutively from women attending the Outpatient Clinics of King Abdulaziz University Hospital. Demographic, anthropometric, and biochemical parameters were recorded. Data were analyzed for women with and without metabolic syndrome.

Results: Abdominal obesity, IR, and hypovitaminosis D were highly prevalent within our population sample. Of the components used to define metabolic syndrome; waist circumference, serum triglycerides (TG), high density lipoprotein-cholesterol, and fasting blood glucose (FBG) were significantly related with all surrogate measures of IR. Significant inverse correlations were found between serum vitamin D and serum TG, FBG, and diastolic blood pressure, within the study cohort.

Conclusions: These observations suggest that hypovitaminosis D may be associated with the risk of developing metabolic syndrome. Interrelationships between IR, metabolic syndrome, and hypovitaminosis D are of particular interest in Saudi population, given the high prevalence of these conditions in this region.

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Introduction

There is increasing interest in the non-skeletal effects of vitamin D and the relationship between vitamin D deficiency and diseases such as obesity, diabetes mellitus, and coronary artery diseases [1].

Abbreviations: 25(OH)D3, 25-Hydroxyvitamin D3; AHA/NHLBI, American Heart Association/National Heart Lung and Blood Institute; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high density lipoprotein-cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IR, Insulin resistance; KAUH, King Abdulaziz University Hospital; LDL-C, low-density lipoprotein-cholesterol; PTH, parathyroid hormone; QUICKI, quantitative insulin sensitivity check index-I; SBP, systolic blood pressure; SD, standard deviation; TG, triglycerides.

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E-mail address: em_alissa@yahoo.com (E.M. Alissa).

Serum 25-hydroxyvitamin D3 (25(OH)D3) concentrations reflect vitamin D status derived from diet, exposure of the skin to sunlight, as well as the conversion of vitamin D from adipose stores in the liver. Therefore, it is considered the most appropriate indicator of overall vitamin D status [2]. Serum concentrations of 25(OH)D < 50 nmol/L are reported to be associated with decreased insulin sensitivity and metabolic syndrome [3].

Insulin resistance (IR) and hyperinsulinemia often precede 2 diabetes [4]. Current interest in IR and metabolic syndrome is because of their increasing prevalence in many populations and the associated high rate of mortality and morbidity due to cardiovascular disease, even in non-diabetic subjects [5]. Previous reports suggest a positive association between IR and markers of inflammation, such as C-reactive protein [6]. It is possible that chronic inflammation may represent a triggering factor in the origin of IR and subsequently type 2 diabetes [7].

The assessment of IR can be made by evaluating the peripheral insulin sensitivity using in vivo methods such as the pancreatic suppression test and the hyperinsulinemic-euglycemic clamp
Venous blood samples were taken from an antecubital vein and by the same trained staff for analysis. To avoid subjective error, all measurements were taken sure (DBP) readings were recorded at 5-min intervals and averaged using a standard mercury sphygmomanometer (Baumanometer, crest (minimum waist).

Although the prevalence of metabolic syndrome in adults living in the Kingdom of Saudi Arabia has been investigated [13], no study has examined the relationship between surrogate measures of IR and metabolic syndrome. Furthermore, it remains uncertain whether the presence of metabolic syndrome and IR are linked to the greater rates of hypovitaminosis D observed in Saudi post-menopausal women [14,15]. Therefore, we aimed to investigate the relationship between HOMA-IR, QUICKI, McAuley indices, and vitamin D deficiency in Saudi post-menopausal women with and without metabolic syndrome.

Methods

The study population consisted of 300 postmenopausal women aged 46–88 years enrolled consecutively from women attending the Outpatient Clinics of King Abdulaziz University Hospital (KAUH) during visits for fitness purposes, or routine checkups, or for evaluation of cardiovascular risk factors.

Postmenopausal status was defined as cessation of menstruation for at least 1 year. None of the patients had any the following disorders: liver or renal disease, inflammatory disease, vascular disease (i.e., peripheral vascular disease, cerebro-vascular disease), endocrine disease, established osteoporosis, or on any form of drug treatment with a possible effect on bone metabolism, including: bisphosphonate, or estrogen replacement therapy, oral contraceptives, statins, aspirin, antioxidants, vitamin D or calcium supplements.

The study was approved by the ethical review board of KAUH. All subjects gave their informed consent for the study, which was performed in accordance with the guidelines proposed in the Declaration of Helsinki.

Participants were questioned about their age, age at the onset of menopause, socioeconomic status, family history of osteoporosis, lifestyle behaviors, including cigarette smoking and physical activity level, and frequency of exposure to sunlight. Smoking habit was categorized as non-smoker, former smoker, and current smoker. Physical activity was self-graded by the participant according to the number of episodes of exercise undertaken per week and were categorized as active (≥3 times/week) or inactive (<3 times/week) according to the recommendations of the American Heart Association consensus statement on primary prevention of coronary diseases and from the USA Surgeon General’s report [16].

Body weight was measured to the nearest 0.1 kg. Height was determined to the nearest cm. Body mass index (BMI) was calculated as the weight (kg) divided by the square of height (m²). Waist circumference was measured at the narrowest part of the abdomen, that is, at the natural indentation between the 10th rib and the iliac crest (minimum waist).

Arterial blood pressure levels were measured in the right arm using a standard mercury sphygmomanometer (Baumanometer, USA). Two systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings were recorded at 5-min intervals and averaged for analysis. To avoid subjective error, all measurements were taken by the same trained staff.

Fasting blood samples were taken after fasting for at least 12 h. Venous blood samples were taken from an antecubital vein and placed into plain, or heparinized tubes. Tubes were centrifuged at 3000–g for 10 min.

Serum fasting blood glucose (FBG), creatinine, and lipids levels (triglycerides (TG), total cholesterol, and high density lipoprotein (HDL)-cholesterol) were determined by an automatic colorimetric method (Ortho-Clinical Diagnostics, Johnson & Johnson Co, USA). Serum low-density lipoprotein (LDL)-cholesterol values were estimated using the following formula: total cholesterol (mmol/L) – HDL-cholesterol (mmol/L) – triglycerides (mmol/L)/2.2. Serum insulin concentrations were measured by radioimmunoassay (DiaSorin, Italy). Serum 25(OH)D was quantified by a chemiluminescence method using a LIASON autoanalyzer (DiaSorinInc, Stillwater, MN, USA) and all samples were analyzed in duplicate. Subjects with serum 25(OH)D levels <50 nmol/L were categorized as having 25(OH)D deficiency [17]. Intact parathyroid hormone (PTH) was measured with an electrochemiluminescent assay using COBAS e411-Hitachi immunoassay analyzer (Roche Diagnostics GmbH, D-68298 Mannheim, Germany).

We used the American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) definition of metabolic syndrome [18]; the presence of abdominal obesity (>88 cm in women) with at least two of the following: 1) high triglycerides (>1.7 mmol/L, [150 mg/dl]), 2) low HDL cholesterol (<1.04 mmol/L [40 mg/dl] in men and <1.29 mm/L [50 mg/dl] in women), 3) high blood pressure (≥130/85 mm Hg or current antihypertensive medications), and 4) high fasting glucose (>6.1 mmol/L [110 mg/dl]).

Indirect indices of insulin resistance include: HOMA-IR, QUICKI, and McAuley formulas. HOMA-IR was calculated from the fasting insulin (µU/ml) × fasting glucose (mmol/L)/22.5. The QUICKI index is based on the logarithmic transformation: 1/(log fasting insulin (µU/ml) + log fasting glucose (mg/dl)). The McAuley index was calculated: exp [2.63 – 0.28 ln (insulin in mU/L) – 0.31 ln (TG in mmol/L)]. Patients were considered as insulin resistant when McAuley index <5.8, HOMA-IR >2.6 and QUICKI <0.33 [12,19]. Also, TG/HDL-C ratio has been reported to be closely related to insulin resistance among nondiabetic individuals [20].

Means and standard deviations (SD) were calculated for continuous variables. Difference between those with metabolic syndrome and non–metabolic syndrome groups was estimated using was analyzed using an independent 2 sample t-test or Mann–Whitney U-test for continuous variables, and the chi-square test for categorical variables. Pearson’s correlations were performed to examine the associations between IR measures and metabolic syndrome components. A multiple stepwise regression analysis was performed to identify variables that independently predicted IR measures. An interaction of independent variables was assessed. All analyses were performed in SPSS (version 21.5). All reported p values were from two-sided tests and compared to a significant level of 5%.

Results

The clinical characteristics of the 300 postmenopausal women are shown in Table 1. The subjects with metabolic syndrome reported a significantly lower level of physical activity compared to the control group (p < 0.05). However, overweight and obesity were also highly prevalent among the group without metabolic syndrome. 41% were overweight and 51% were obese according to BMI values and 65% had waist circumference >88 cm. Most participants were poorly educated housewives, living in apartments, and had limited exposure to ultraviolet sunlight. Physical inactivity was more prevalent among women with metabolic syndrome than those without metabolic syndrome (46% vs. 32%; p < 0.05) whereas more women without metabolic syndrome were exercising ≥3
times per week than their counterparts with metabolic syndrome (51% vs. 30%; \( p < 0.05 \)).

In our cohort, 57% of subjects met diagnostic criteria for metabolic syndrome displaying higher body weight, BMI, waist circumference, SBP, and DBP values \( (p < 0.01) \). In addition, the metabolic syndrome group had higher serum TG, FOG, insulin, HOMA-IR, QUICK-I, and McAuley index levels \( (p < 0.001) \) as compared to the non–metabolic syndrome group despite similar serum cholesterol levels (Table 2). There was a wide range for the IR measures in the entire cohort; HOMA-IR \((0.3–36.7)\), QUICK-I \((0.24–4.8)\), and McAuley index \((2.6–13.3)\). Our results showed that 64% of total population was IR according to HOMA-IR index, 70% were IR according to QUICK-I, and 47% were IR according to McAuley index. Those in the metabolic syndrome group had a mean TG/HDL ratio that was almost double the value of those in the non-metabolic syndrome group \( (p < 0.0001) \).

Bivariate correlations between IR measures and components of the metabolic syndrome were evaluated for the whole population (Table 3). HOMA-IR index was related to a greater number of the metabolic syndrome components than the other 2 IR measures. QUICK-I index presented fewer significant, but less strong, correlations with the remaining IR measures. The HOMA-IR index was positively associated with waist circumference \((r = 0.213, p < 0.05)\) and serum TG \((r = 0.307, p < 0.0001)\) and negatively associated with serum HDL-C \((r = -0.202, p < 0.05)\). QUICK-I index was negatively associated with waist circumference \((r = -0.285, p < 0.0001)\), TG \((r = -0.311, p < 0.0001)\), FOB \((r = -0.556, p < 0.0001)\), and positively associated with HDL-C \((r = 0.211, p < 0.05)\).

### Table 1

Clinical characteristics according to the presence or absence of metabolic syndrome in 300 postmenopausal women

|                                      | Postmenopausal women without MetS \((n = 129)\) | Postmenopausal women with MetS \((n = 171)\) | \( p \) value |
|--------------------------------------|------------------------------------------------|------------------------------------------------|--------------|
| Age (years)                          | 59.4 ± 0.8                                     | 60.3 ± 0.6                                      | 0.491        |
| Age at menopausal (years)            | 49.9 ± 0.5                                     | 50.5 ± 0.4                                      | 0.722        |
| Body weight (kg)                     | 72.2 ± 1.3                                     | 77.6 ± 1.1                                      | <0.0001      |
| Body height (cm)                     | 151.7 ± 0.5                                    | 152.9 ± 0.4                                     | 0.061        |
| BMI (kg/m²)                          | 31.3 ± 0.5                                     | 33.2 ± 0.4                                      | 0.001        |
| BMI classes                          |                                               |                                                | 0.005        |
| Normal (18.5 kg/m²–24.9 kg/m²)       | 10 (8)                                         | 9 (5)                                           |             |
| Overweight (25 kg/m²–29.99 kg/m²)    | 54 (41)                                        | 43 (25)                                         |             |
| Obese (>30 kg/m²)                    | 65 (51)                                        | 119 (70)                                        |             |
| Waist circumference (cm)             | 95.8 ± 1.4                                     | 103.2 ± 1.7                                     | <0.0001      |
| Waist circumference classes          |                                               |                                                | <0.0001      |
| Waist circumference >88 cm           | 83 (65)                                        | 171 (100)                                       |             |
| SBP (mm Hg)                          | 128.0 ± 1.9                                    | 140.5 ± 0.9                                     | <0.0001      |
| DBP (mm Hg)                          | 76.3 ± 1.0                                     | 79.9 ± 1.0                                      | 0.007        |
| Marital status                       |                                               |                                                | <0.05        |
| Married                              | 72 (56)                                        | 107 (63)                                        |             |
| Widowed                              | 33 (25)                                        | 53 (31)                                         |             |
| Divorced                             | 24 (19)                                        | 11 (6)                                          |             |
| Parity                               |                                               |                                                | 0.278        |
| 0                                    | 5 (4)                                          | 9 (5)                                           |             |
| 1                                    | 3 (2)                                          | 4 (4)                                           |             |
| 2                                    | 2 (1)                                          | 4 (2)                                           |             |
| 3                                    | 10 (8)                                         | 6 (4)                                           |             |
| ≥4                                   | 109 (85)                                       | 148 (87)                                        |             |
| Education level                      |                                               |                                                | 0.161        |
| Illiterate                           | 53 (41)                                        | 89 (52)                                         |             |
| Intermediate                         | 41 (32)                                        | 37 (22)                                         |             |
| High school                          | 10 (7)                                         | 19 (11)                                         |             |
| University                           | 25 (20)                                        | 26 (15)                                         |             |
| Occupation                           |                                               |                                                | 0.158        |
| House wife                           | 121 (93)                                       | 167 (98)                                        |             |
| Administrative                       | 6 (5)                                          | 2 (1)                                           |             |
| Director/physician                   | 2 (2)                                          | 2 (1)                                           |             |
| Type of residency                    |                                               |                                                | 0.545        |
| Traditional housing                  | 26 (20)                                        | 37 (22)                                         |             |
| Apartment                            | 79 (62)                                        | 103 (60)                                        |             |
| Villa                                | 24 (19)                                        | 31 (18)                                         |             |
| Exposure to sunlight                 |                                               |                                                | 0.222        |
| <1 time                              | 89 (70)                                        | 129 (75)                                        |             |
| 1–2 times                            | 37 (28)                                        | 32 (19)                                         |             |
| >3 times                             | 3 (2)                                          | 10 (6)                                          |             |
| Veil type                            |                                               |                                                | 0.336        |
| Covering hair only                   | 37 (28)                                        | 52 (30)                                         |             |
| Eyes shown only                      | 85 (66)                                        | 104 (61)                                        |             |
| Full cover                           | 7 (6)                                          | 15 (9)                                          |             |
| Physical activity                    |                                               |                                                | 0.033        |
| <1 time                              | 41 (32)                                        | 78 (46)                                         |             |
| 1–2 times                            | 23 (17)                                        | 33 (19)                                         |             |
| >3 times                             | 65 (51)                                        | 60 (35)                                         |             |
| Smoking status                       |                                               |                                                | 0.826        |
| Non-smoker                           | 120 (94)                                       | 161 (94)                                        |             |
| Former smoker                        | 3 (2)                                          | 6 (4)                                           |             |
| Current smoker                       | 6 (4)                                          | 4 (2)                                           |             |

Data are given as the mean ± SD or as the number of subjects with percentages given in parentheses, as appropriate. Categorical data are compared by \( \chi^2 \) test, continuous variables are compared by unpaired \( t \)-test. BMI: body mass index, DBP: diastolic blood pressure, SBP: systolic blood pressure.
measures and metabolic syndrome components. Significant insulin sensitivity check index, SBP: systolic blood pressure, TC: total glucose, HDL-C: high density lipoprotein-cholesterol, HOMA-IR: homeostasis model in bold font. BMI: body mass index, DBP: diastolic blood pressure, FBG: fasting blood glucose, HDL-C: high density lipoprotein-cholesterol, HOMA-IR: homeostasis model for insulin resistance, LDL-C: low density lipoprotein-cholesterol, QUICK-I: quantitative insulin sensitivity check index, TC: total cholesterol, TG: triglycerides.

Because various factors could affect IR measures, we performed multivariate regression analyses and included all potential covariates (Table 4). The first model confirmed an independent relationship between serum levels of TG, FBG, insulin, and QUICK-I with HOMA-IR accounting for 90.0% of the variation. The second model showed that serum TG, HDL-C, TG/HDL-C, FBG, and QUICK-I levels were significant independent predictors of McAuley index ($R^2 = 94.2\%$). As shown in the third model serum TG, HDL-C, TG/HDL-C, FBG, McAuley index, and HOMA-IR were highly significant and independent predictors for QUICK-I, it accounted for 94.1% of the variation.

Vitamin D deficiency was identified in 80% of the entire cohort but was more prevalent in the metabolic syndrome group compared to the non-metabolic syndrome group (82% vs. 77%) without a statistically significant difference in the mean values of serum vitamin D ($p > 0.05$). The relationship between serum vitamin D concentrations to insulin sensitivity was investigated in the study cohort. There was a significant inverse correlation between serum vitamin D with 3 components of the metabolic syndrome; serum TG ($r = -0.183$, $p < 0.05$), FBG ($r = -0.192$, $p < 0.05$), and DBP ($r = -0.130$, $p < 0.05$) levels. In addition, serum vitamin D was positively correlated with McAuley index ($r = 0.167$, $p < 0.05$). However, this association was not significant after multivariate analysis. No significant correlations were observed between serum vitamin D concentration and either HOMA-IR or QUICK-I. Of all these variables, DBP was shown to be the only predictive variable, accounting for 1.4% of variation in serum vitamin D concentrations ($\beta = -0.118$, $p < 0.05$). However, the prevalence of IR was significantly higher ($p < 0.05$) among vitamin D deficient women, as categorized by serum circulating levels $<50$ nmol/L, by all IR measures ($64\%$ according to HOMA-IR, $70\%$ according to QUICK-I, and $48\%$ according to McAuley index).

**Discussion**

The results presented show that abdominal obesity, IR, and hypovitaminosis D were highly prevalent among our cohort of 300 postmenopausal women with and without metabolic syndrome as

### Table 2

| Predictor variable | $\beta$ | $p$ | 95% CI for $\beta$ |
|-------------------|--------|-----|------------------|
| HOMA-IR: Serum insulin | 0.891 | $<0.0001$ | 0.394, 0.451 |
| QUICK-I: Serum TG | -0.064 | 0.001 | -0.540, -0.132 |
| QUICK-I: Serum FBG | 0.525 | 0.001 | 0.806, 0.967 |
| QUICK-I: Serum TG | 0.177 | $<0.0001$ | 14.02, 34.245 |
| QUICK-I: Serum FBG | -0.484 | $<0.0001$ | -0.007, -0.005 |
| McAuley index: Serum FBG | 0.619 | 0.001 | 0.020, 0.027 |
| McAuley index: Serum HDL-C | -0.105 | $<0.0001$ | -0.017, -0.007 |
| McAuley index: Serum HOMA-IR | 0.205 | 0.001 | 0.001, 0.002 |
| McAuley index: Serum McAuley index | 0.885 | $<0.0001$ | 0.019, 0.021 |
| QUICK-I: Serum HDL-C | -0.256 | $<0.0001$ | 0.011, -0.005 |
| QUICK-I: Serum HOMA-IR | 0.205 | 0.001 | 0.001, 0.002 |
| QUICK-I: Serum McAuley index | -0.825 | $<0.0001$ | 0.364, 0.397 |

95% CI: confidence intervals, $\beta$: standardized regression coefficient, FBC: fasting blood glucose, HDL-C: high density lipoprotein-cholesterol, HOMA-IR: homeostasis model for insulin resistance, QUICK-I: quantitative insulin sensitivity check index, $R^2$: percent variance explained by each variable, TC: total cholesterol, TG: triglycerides.
defined by the AHA/NHLBI. The high prevalence of metabolic syndrome observed in our cohort may have obscured the impact of other coronary risk factors. Whilst none of the subjects had clinical evidence of hypertension, diabetes, coronary artery disease, or dyslipidemia (according to the cutoff values of the AHA/NHLBI definition of metabolic syndrome), which although are not apparent at current presentation may appear later in life. Several of these conditions are known to influence insulin sensitivity [21], for example abdominal obesity which is also an important coronary risk factor, both directly and through its association with other coronary risk factors [22]. The presence of IR itself appears to be the result of a complex interplay of genetic factors with environmental factors. Taking these findings for the majority of the study cohort together with their old age, sedentary lifestyle habits, low to middle socioeconomic status, and limited exposure to sunlight, it may be linked to the presence of IR as well as hypovitaminosis D. Since it has been proposed that 25(OH)D deficiency was associated with decreased peripheral insulin action, either via reduced insulin receptor expression or via impaired signaling downstream of the insulin receptor [23].

Metabolic syndrome is defined by a clustering of cardiovascular risk factors that include central adiposity, hypertension, dyslipidemia and impaired glucose metabolism. Indeed IR is considered the key feature of metabolic syndrome and is associated with several component features of metabolic syndrome [21]. Of these component features; waist circumference, serum TG, HDL-C, and FBG were significantly related to all surrogate measures of IR. The relationship with serum TG, HDL-C, and FBG were independent of confounding factors with at least 2 IR measures. Thus our data suggest that surrogate markers of IR may help to identify subjects with some components of the metabolic syndrome and who may be at high future risk of metabolic imbalances. Similar results have been reported previously [24]. Even though the authors did not include plasma insulin and glucose values in the regression analysis, as they were already included in the HOMA-IR formula. Identifying subjects with IR is difficult because insulin sensitivity is difficult to quantify accurately. Therefore, early screening of IR using any of the surrogate markers might be useful in a high-risk population (for example our cohort of postmenopausal women) who are at increased risk of developing diabetes. Strong independent correlations between the 3 IR indices also suggest validity of all these measures of IR. Multivariate analysis has previously shown that TG is an independent predictor of the 3 IR measures. Hypertriglyceridemia is closely linked to IR [25].

Vitamin D can affect tissues that are not involved in calcium homeostasis and bone metabolism, such as its immune modulatory functions and its implication in systemic inflammation [23,26]. Therefore, vitamin D deficiency is proposed to be a risk factor for a number of conditions. Furthermore, vitamin D could play a role in the pathogenesis of type 2 diabetes, by affecting insulin sensitivity [27,28]. Inverse correlations were demonstrated between serum vitamin D with 3 components of metabolic syndrome; serum TG, FBG, and DBP, amongst the whole population. These observations indicate that hypovitaminosis D is associated with an increased risk of metabolic syndrome. Similar results have been found in postmenopausal women confirming an association of vitamin D status with metabolic syndrome [29]. Other studies failed to show a significant association between vitamin D and metabolic syndrome [30]. DBP accounted for 1.4% of changes in serum vitamin D level (β = -0.118, p < 0.05). It has been reported previously that cardiovascular disease and hypertension are related to serum Vitamin D status [31]. There is also a growing evidence that vitamin D has a preventive role in the development of heart disease [32].

It appears that vitamin D may stimulate the expression of the insulin receptor in peripheral tissues and thereby increase glucose transport [33]. Insulin-mediated processes are calcium dependent and therefore may be indirectly influenced by vitamin D status [34]. There is some evidence suggesting that vitamin D deficiency might be involved in the pathogenesis of insulin resistance and the metabolic syndrome [1,35]. However the exact mechanisms remain unknown. Inflammation is believed to accelerate the pathogenesis of metabolic syndrome and through local activation of 25(OH)D to its active form by tissue macrophages, which can open calcium channels and lead to calcification in vascular smooth muscle cells [36]. Calcium ion fluxes have an important role in regulating secretory mechanisms including insulin secretion. Vitamin D may play a role in the regulation of β-cell function [23]. Others have suggested vitamin D deficiency and the associated secondary hyperparathyroidism, are among endocrine derangements of obesity, to be implicated as risk factors for metabolic syndrome [37].

IR is a complex disorder that has recently been proposed to be important in the pathogenesis of a number of conditions other than metabolic syndrome, including hypovitaminosis D [35]. Data from the Framingham Offspring Study show an inverse association of 25(OH)D with HOMA-IR index in non-diabetic adults [38]. In our study, subjects in the vitamin D deficient group had a significantly higher prevalence of IR than the vitamin D sufficient group (p < 0.05). Thus, hypovitaminosis D may be linked to IR and the variables that can integrate the abnormalities of the metabolic syndrome and cardiometabolic function. The McAuley index was the only IR measure showing positive correlation with serum vitamin D. However, this association lost significance in the multiple regression analysis, suggesting either the absence of an association between these two variables or insufficient power of our study to detect an existing association.

Because of our cross-sectional study design the causality of relationships between parameters cannot be proven; a future longitudinal study that addresses the association of insulin resistance with hypovitaminosis D may therefore be of value. It should also be noted that all IR surrogate markers are based on the estimation of insulin effects on glucose metabolism which do not always assess the broader metabolic consequences of insulin resistance, e.g. abnormalities in lipid metabolism. Furthermore, the different definitions of the metabolic syndrome have led to some confusion and inconsistency between studies. One difficulty has been that the conceptual framework used to define metabolic syndrome has not been agreed. Given the high mean fasting blood glucose value among postmenopausal women with metabolic syndrome, it would have been useful to conduct oral glucose tolerance test, or hemoglobin A1c to make a formal diagnosis of diabetes mellitus in our study population.

Interrelationships among IR, metabolic syndrome, and hypovitaminosis D are of particular interest in the Saudi population. Because of the high prevalence of diabetes in this population and the high risk of cardiovascular diseases among those with diabetes, the need for early cardiovascular risk factor modification is greatly increased. In conclusion, our findings suggest that hypovitaminosis D might be an important factor in IR and metabolic syndrome. In Saudi Arabia, postmenopausal women, may be at risk of inadequate vitamin D status because of limited exposure to sunlight and, lower dietary intake [1].

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