Journal of Biosciences and Medicines, 2025, 13(12), 210-223
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Endothelial Adhesion Molecules as Early Predictors of Metabolic Syndrome in Young Adults

Santiago Cristóbal Sigrist-Flores[1,2*], Miguel Ángel Espinoza-Camacho[3], Adolfo René Méndez-Cruz[2], José Rafael Jiménez-Flores[2], Rafael Villalobos-Molina[1,4], Itzell Alejandrina Gallardo-Ortíz[1,4]

[1]Unidad de Biomedicina, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, Tlalnepantla, México
[2]Carrera de Médico Cirujano, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, Tlalnepantla, México
[3]Unidad Académica Profesional Acolman, Universidad Autónoma del Estado de México, UAEMEX, Acolman, México
[4]Carrera de Enfermería, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, Tlalnepantla, México
Email: *santiago_sigrist@iztacala.unam.mx

How to cite this paper: Sigrist-Flores, S.C., Espinoza-Camacho, M., Méndez-Cruz, A.R., Jiménez-Flores, J.R., Villalobos-Molina, R. and Gallardo-Ortíz, I.A. (2025) Endothelial Adhesion Molecules as Early Predictors of Metabolic Syndrome in Young Adults. *Journal of Biosciences and Medicines*, **13**, 210-223.
https://doi.org/10.4236/jbm.2025.1312016

Received: October 19, 2025
Accepted: December 12, 2025
Published: December 15, 2025

Abstract

Background: Metabolic Syndrome (MetS) shows a high prevalence among young Mexican adults, and its metabolic impairments are difficult to reverse once established. Identifying early biomarkers of endothelial dysfunction may enable timely prevention. **Objective:** This study evaluated whether circulating adhesion molecules act as early indicators of metabolic risk in apparently healthy young adults. **Methods:** We analyzed serum concentrations of sVCAM-1, sICAM-1, and sE-selectin, along with adiponectin, resistin, and leptin, in 503 university students (283 women and 220 men; mean age 19 years). Adhesion molecules were compared across three groups (Control, 1 - 2 alterations, and MetS), and adipokines were evaluated in Control and MetS groups. **Results:** sICAM-1 and sE-selectin were significantly higher in MetS than in Control and 1 - 2 alterations groups, in both sexes; notably, sICAM-1 was already elevated in men with only 1 - 2 alterations. Leptin was higher in men with MetS, whereas adiponectin was significantly reduced in women with MetS, and showed a non-significant decreasing trend in men. Resistin showed no significant differences in either sex. These findings indicate that sICAM-1 and sE-selectin function as early biomarkers of endothelial dysfunction in young adults and that their combined evaluation improves diagnostic performance. The more pronounced alterations observed in men highlight a sex-specific vulnerability that should be considered when defining diagnostic thresholds. **Conclusions:**

Overall, the simultaneous assessment of these markers may support early screening strategies and inform sex-aware preventive interventions. Longitudinal studies are warranted to validate predictive value and define their implementation in clinical and public-health settings.

Keywords

Endothelium, Adhesion Molecules, Metabolic Syndrome, Young Adults

1. Introduction

The mechanisms linking obesity, inflammation, and their complications remain only partially understood. Over the last decade, evidence has consolidated the concept that obesity represents a state of chronic, low-grade inflammation that mediates the connection between excess adiposity, insulin resistance, endothelial dysfunction, and the development of Metabolic Syndrome (MetS) [1] [2]. MetS is characterized by the coexistence of several metabolic risk factors including visceral obesity, dyslipidemia, hyperglycemia and elevated blood pressure that, together, increase the likelihood of developing cardiovascular disease, type 2 diabetes, reproductive disorders, and certain types of cancer [3] [4]. The inflammatory response initiated in white adipose tissue contributes to systemic low-grade inflammation, where adipocytes and infiltrated immune cells release adipokines and cytokines—such as adiponectin, resistin, leptin, and C-Reactive Protein (CRP)—that regulate inflammatory signaling and perpetuate a chronic cycle leading to insulin resistance, and atherosclerosis [3] [4]. MetS is therefore recognized as a chronic inflammatory condition characterized by elevated CRP, Interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) [5]-[7]. Nonetheless, inflammation and metabolic markers are not always concordant: some obese individuals exhibit normal cytokine profiles, whereas some lean subjects with hypertension or type 2 diabetes show increased inflammatory mediators [5] [7]. This variability suggests that endothelial dysfunction may occur early in the MetS pathophysiological continuum, preceding overt clinical manifestations.

Recent evidence supports endothelial activation as one of the earliest detectable events in metabolic dysregulation. The upregulation of adhesion molecules—such as E-selectin, Vascular Cell Adhesion Molecule-1 (VCAM-1), and Intercellular Adhesion Molecule-1 (ICAM-1)—facilitates leukocyte attachment and transmigration across the vascular wall, promoting a pro-inflammatory and pro-atherogenic environment [5] [6] [8]. Elevated plasma concentration of their soluble forms (sE-selectin, sVCAM-1, sICAM-1) serves as an early indicator of endothelial perturbation, and correlates with the severity of MetS and cardiovascular risk [5] [7] [9]. Adipokines further modulate endothelial inflammation: adiponectin exerts protective and anti-inflammatory effects, whereas leptin and resistin promote adhesion-molecule expression, endothelial dysfunction, and oxidative stress [2] [4] [9]. This complex interaction between adipokines and adhesion molecules

underlies the systemic inflammatory milieu characteristic of MetS. However, most available studies have been conducted in adults with advanced metabolic alterations. Little is known about the early inflammatory and endothelial changes occurring in young, apparently healthy individuals, despite their increasing exposure to risk factors such as sedentary lifestyle and high-calorie diets [9] [10]. The evaluation of endothelial adhesion molecules and adipokines could, therefore, help identify early biomarkers of metabolic imbalance in this population. This study aimed to evaluate the serum values of endothelial adhesion molecules (sVCAM-1, sICAM-1, sE-selectin) and adipokines (adiponectin, resistin, leptin) in young adults with and without diagnostic criteria for MetS, to identify potential early endothelial biomarkers of metabolic syndrome in an apparently healthy young population [8]-[11].

2. Materials and Methods

2.1. Study Population and Ethical Statement

A total of 503 blood samples were obtained from young Mexican adults (283 women and 220 men; mean age 19 years). All participants were first-year undergraduate students at the National Autonomous University of Mexico (UNAM), FES Iztacala campus, located in the northern area of the Mexico City metropolitan region. Participants self-reported as healthy and provided written informed consent prior to enrollment. For the purposes of this study, "apparently healthy" was operationally defined as having no known chronic diseases (e.g., diabetes, hypertension, dyslipidemia), no prior diagnosis of metabolic or cardiovascular disorders, and not taking any medication for metabolic, endocrine, or inflammatory conditions at the time of recruitment. The research protocol was approved by the Institutional Ethics Committee of FES Iztacala, UNAM, and conducted in accordance with the Declaration of Helsinki [8].

2.2. Diagnostic Criteria for Metabolic Syndrome

Metabolic Syndrome (MetS) was defined according to the International Diabetes Federation/American Heart Association criteria [8] [12]. Participants were classified into three groups based on the number of altered parameters: Control: no metabolic alteration; 1 - 2 alterations: one or two altered parameters; MetS: three or more altered parameters.

An altered parameter was recorded when the corresponding categorical cut-off was met, as follows:

Parameter	Categorical cut-off point
HDL-Cholesterol	<50 mg/dL in women <40 mg/dL in men
Waist circumference	≥80 cm in women ≥90 cm in men
Triglycerides	≥150 mg/dL

Continued

Blood pressure	≥130 mm Hg systolic ≥85 mm Hg diastolic
Fasting glucose	≥100 mg/dL

Participants meeting ≥ 3 altered parameters were assigned to the MetS group.

2.3. Laboratory Procedures

All blood samples were obtained between 08:00 and 10:00 h after a 12-hour overnight fast. Venous blood was collected into Vacutainer® serum-separation tubes (SST, yellow cap) containing a polymer gel separator. Samples were allowed to clot at room temperature for 20 - 30 minutes, kept protected from light, and centrifuged at 1500 ×g for 10 minutes at 4˚C to separate the serum fraction.

Serum was carefully collected, aliquoted into sterile polypropylene vials, and immediately stored at –80˚C until analysis. No freeze-thaw cycles were permitted. Concentrations of soluble adhesion molecules (sVCAM-1, sICAM-1, and sE-selectin) and adipokines (adiponectin, resistin, and leptin), were quantified using commercial ELISA kits (Invitrogen™, Waltham, MA, USA). Adhesion molecules were measured with the following kits: sVCAM-1 (Cat. KHT0601), sICAM-1 (Cat. BMS241), and sE-selectin (Cat. BMS205-2). Adipokines were measured using adiponectin (Cat. BMS2032-2), resistin (Cat. BMS2040), and leptin (Cat. KAC2281) ELISA kits. All assays were performed according to the manufacturer's instructions. Samples were analyzed in duplicate, and absorbance was read using a microplate spectrophotometer (BioTek™ ELx800, USA). Intra-assay and inter-assay coefficients of variation were <10% for all analytes.

2.4. Statistical Analysis

Data were analyzed using GraphPad Prism version 9.0 (GraphPad Software, San Diego, CA, USA). Normality of data distribution was evaluated using the Shapiro–Wilk test. Since most variables met normality assumptions, comparisons among the three groups ("Control", "1 - 2 alterations", and "MetS") were performed using a one-way analysis of variance (one-way ANOVA). When significant differences were detected, Tukey's multiple comparison test was applied as the post hoc procedure to determine pairwise group differences. For adipokines, which were analyzed only between Control and MetS groups, comparisons were performed using an unpaired two-tailed Student's *t*-test. A p value ≤ 0.05 was considered statistically significant.

Receiver Operating Characteristic (ROC) curves were constructed to determine optimal cut-off points for sICAM-1 and sE-selectin separately for men and women. Sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) were calculated using standard formulas. A p value ≤ 0.05 was considered statistically significant.

3. Results

3.1. General Characteristics of the Study Population

A total of 503 young adults were included (283 women and 220 men; mean age 19.0 years, range 17 - 24 years). Based on the number of altered metabolic parameters, 157 participants (31.2%) were classified as Healthy, 188 (37.4%) as having 1 - 2 alterations, and 158 (31.4%) as meeting criteria for MetS. Across individual components, Waist Circumference (WC) and low HDL-C were the most prevalent abnormalities overall (47.5% and 47.3%, respectively), followed by hypertriglyceridemia (33.8%), impaired fasting glucose (20.3%), and elevated blood pressure (14.1%). Sex-specific patterns were evident: women more frequently presented low HDL-C (58.3% vs. 33.2% in men) and elevated WC (53.4% vs. 40.0%), whereas men more often showed elevated blood pressure (19.5% vs. 9.9% in women) and slightly higher elevated glucose (21.8% vs. 19.1%); triglycerides were similar between sexes (33.9% in women vs. 33.6% in men) (Table 1, Table 2).

The distribution of individual MetS components showed that alterations in Waist Circumference (WC) and High-Density Lipoprotein-Cholesterol (HDL-C) were the most prevalent abnormalities among both sexes, followed by changes in Triglycerides (TG), and Glucose (GLU) values.

Table 1. Characteristics of the sample.

	Total	Healthy	1 - 2 alterations	MetS	Age (years) Average	Age range (Min-Max)
Women (n)	283	77	110	96	19.0	17 - 24
Men (n)	220	80	78	62	19.0	17 - 24
Total young (n)	503	157	188	158	-	-

Table 2. Distribution of altered MetS components by sex.

	Women (n)			Men (n)		
	Not Altered	Altered	% Altered	Not Altered	Altered	% Altered
Waist Circumference (WC)	132	151	53.4%	132	88	40.0%
Glucose (GLU)	229	54	19.1%	172	48	21.8%
Blood Pressure (BP)	255	28	9.9%	177	43	19.5%
Triglycerides (TG)	187	96	33.9%	146	74	33.6%
High-Density Lipoprotein-Cholesterol (HDL-C)	118	165	58.3%	147	73	33.2%

(Global altered totals: WC 239/503 = 47.5%; HDL-C 238/503 = 47.3%; TG 170/503 = 33.8%; GLU 102/503 = 20.3%; BP 71/503 = 14.1%).

3.2. Adhesion Molecules

The soluble fractions of the endothelial adhesion molecules differed significantly

across groups (Figure 1). Mean plasma concentrations of sICAM-1 and sE-selectin were higher in participants with MetS than in both the Control and 1 - 2 alterations groups, in women and men ($p \leq 0.05$). In addition, sICAM-1 values were already elevated in men with 1 - 2 alterations compared with healthy controls ($p \leq 0.05$). Taken together, these patterns of early increases in sICAM-1 with emerging abnormalities and marked sE-selectin elevations in overt MetS support their potential utility as early endothelial biomarkers of metabolic syndrome.

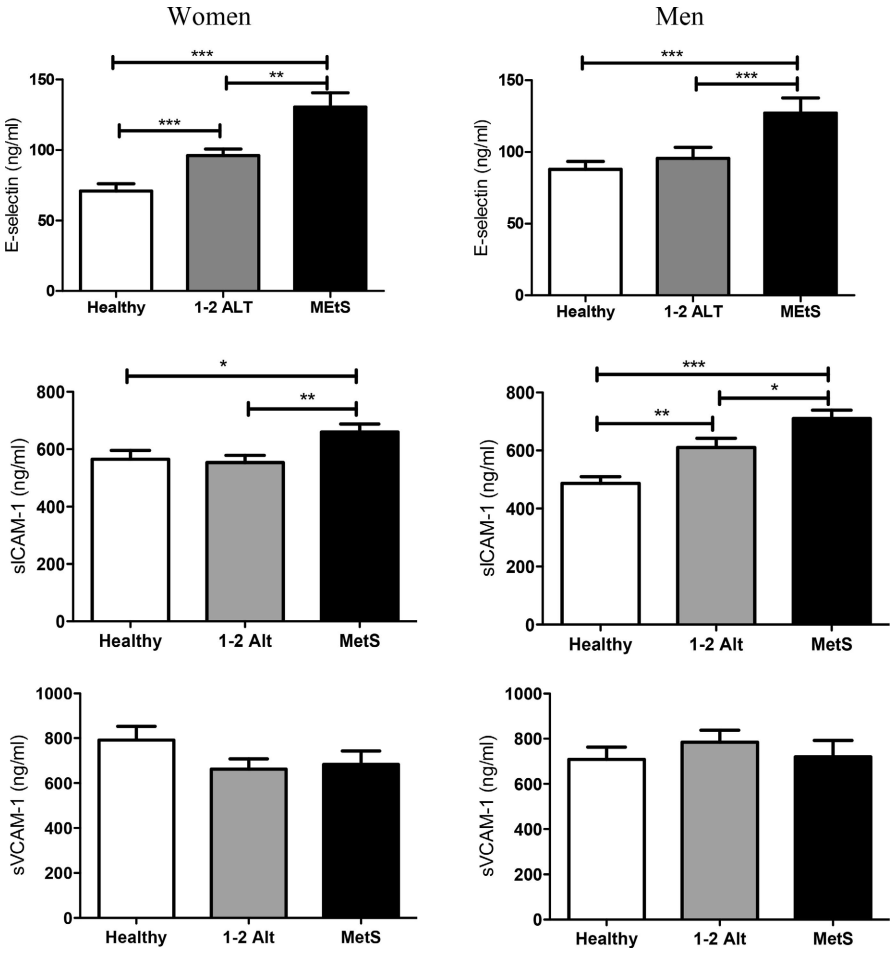

Figure 1. Mean (±SEM) plasma concentrations of soluble endothelial adhesion molecules sVCAM-1, sICAM-1, and sE-selectin across metabolic groups: Control (no altered MetS components), 1 - 2 Alt (one or two altered components), and MetS (≥3 altered components). Group differences were tested by ANOVA with Tukey post hoc. Significance levels: $p \leq 0.05$ (*), $p \leq 0.001$ (**), $p \leq 0.0001$ (***).

3.3. Adipokines

Mean serum concentrations of adipokines are shown in Figure 2. In men, leptin values were significantly higher in the MetS group compared with Controls ($p \leq 0.05$), indicating an early shift toward a pro-inflammatory adipokine profile. Adiponectin exhibited a non-significant decreasing trend in both sexes, whereas resistin concentrations did not differ between Control and MetS groups. Among

women, no significant differences were observed for adiponectin, resistin, or leptin. Overall, these results suggest that adipokine alterations are more evident in young men with early metabolic impairment, while women showed a more preserved adipokine profile at this stage.

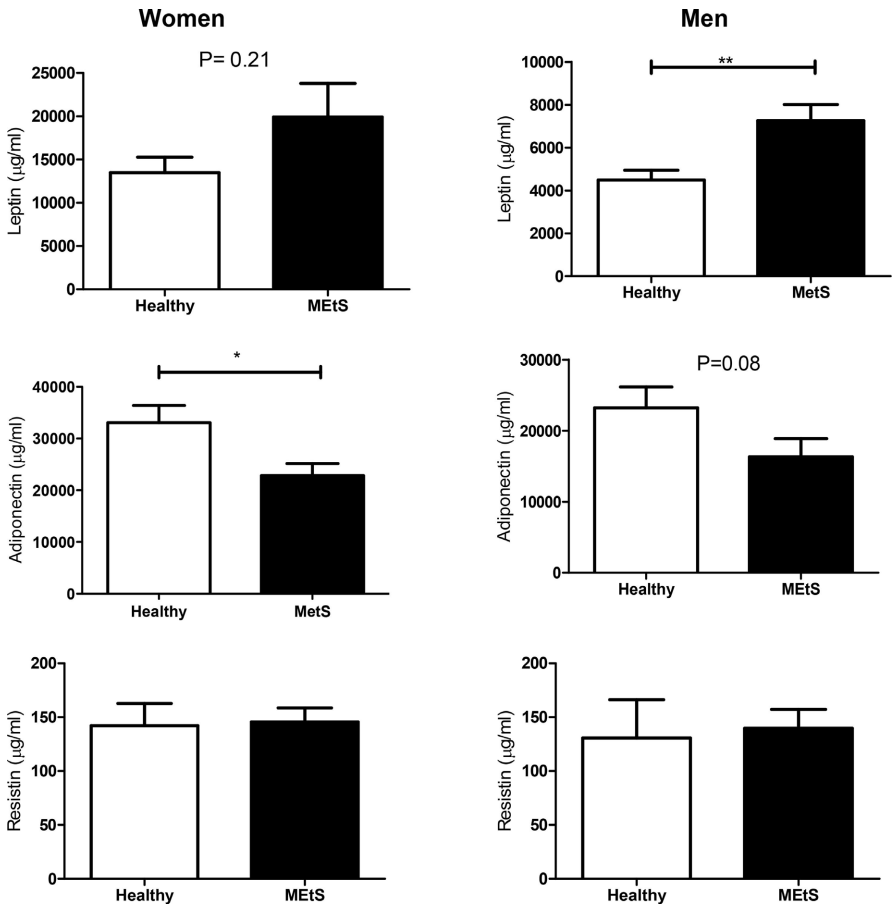

Figure 2. Mean (±SEM) plasma concentrations of adipokines—adiponectin, resistin, and leptin—in young adults by metabolic status: Control (no altered MetS components) and MetS (≥3 altered components). Between-group differences were assessed by *t*-test. Significance: $p \leq 0.05$.

3.4. Sensitivity and Specificity Analyses

Receiver Operating Characteristic (ROC) analyses were performed to derive sex-specific cut-off points for sE-selectin and sICAM-1 as candidate biomarkers of metabolic alterations (Table 3 and Table 4). For sE-selectin, a threshold of 102 ng/mL provided high specificity (women, 86%; men, 71%) with modest sensitivity (women, 38%; men, 42%). For sICAM-1, cut-off of 700 ng/mL (women) and 760 ng/mL (men) yielded specificities of 84% and 93%, respectively, with sensitivities of 28% and 27%. Despite limited sensitivity, both markers showed favorable Positive Predictive Values (PPV): 72% - 78%, supporting their potential utility to rule in metabolic alterations in young adults.

Table 3. Number of young adults classified by concentration of E-Selectin and sICAM (*cut-offs from ROC*; *count by sex*).

	Women			Men		
	Cut-off point	Healthy	1 - 2 alterations	Cut-off point	Healthy	1 - 2 alterations
E-Selectin (ng/ml)	<102	36	34	<102	29	19
	≥102	6	21	≥102	12	14
sICAM (ng/ml)	<700	66	89	<760	74	57
	≥700	11	21	≥760	6	21

Table 4. Diagnostic parameters for sE-selectin and sICAM at the selected cut-offs (*cut-offs from ROC*; *count by sex*).

	Women	**Men**
E-Selectin (ng/ml)		
Cutt-off point	102 ng/ml	102 ng/ml
Specificity	86%	71%
Sensitivity	38%	42%
Positive Predictive Value (PPV)	78%	54%
Negative Predictive Value (NPV)	51%	60%
sICAM (ng/ml)		
Cutt-off point	700 ng/ml	760 ng/ml
Specificity	84%	93%
Sensitivity	28%	27%
Positive Predictive Value (PPV)	72%	78%
Negative Predictive Value (NPV)	45%	56%

4. Discussion

Metabolic Syndrome (MetS) represents the convergence of multiple metabolic abnormalities that substantially increase the risk of Type 2 Diabetes (T2D), and cardiovascular disorders [1] [3] [7] [8] [12]. Over the last decade, most studies have either described the prevalence of MetS in different populations or examined molecular alterations associated with its clinical expression [8] [12] [13]. However, the majority have focused on middle-aged or older adults in whom metabolic disturbances are already established, whereas research into early endothelial and inflammatory changes in young, apparently healthy individuals remains limited.

Early identification of biological alterations preceding overt MetS is crucial for prevention. Our group previously reported a 14.4% prevalence of MetS in asymptomatic young Mexican adults, underscoring the relevance of studying this population [13]. The present work expands these findings by demonstrating that endothelial adhesion molecules—particularly sICAM-1 and E-selectin—are already elevated at early stages of metabolic imbalance, supporting their utility as candidate biomarkers of early endothelial activation.

Endothelial dysfunction is widely recognized as an initiating and central event

in the pathophysiology of MetS and its cardiovascular complications. It is characterized by reduced Nitric Oxide (NO) bioavailability, an imbalance between vasodilatory and vasoconstrictive factors, and heightened vascular inflammation and oxidative stress [10] [11]. Emerging evidence suggests that endothelial dysfunction is not only a consequence of metabolic alterations but also a precipitating factor, linking insulin resistance and vascular injury through shared inflammatory and oxidative pathways [11] [14]. Mechanistically, mitochondrial oxidative stress, activation of pro-inflammatory signaling cascades (e.g., NF-κB, MAPK), and impaired calcium-dependent endothelial responses contribute to the upregulation of adhesion molecules (E-selectin, ICAM-1, VCAM-1), promoting leukocyte adhesion and transmigration and amplifying vascular inflammation [5] [6].

Contemporary reviews highlight that these adhesion molecules function as early biomarkers of endothelial stress, with chronic oxidative and mitochondrial dysfunction driving their elevation before overt structural vascular damage occurs [15]. Ray *et al.* (2023) also reported that impaired flow-mediated dilation, accompanied by increased adhesion molecules, constitutes an early indicator of endothelial activation in cardiometabolic diseases [14]. Clinical studies further reinforce this concept: metabolically healthy individuals with obesity exhibit higher concentrations of sICAM-1 and sE-selectin than metabolically healthy, non-obese controls [16], and in T2D these markers correlate with poor glycemic control and endothelial dysfunction [17] [18]. In young adults, elevated adhesion molecules have been linked to early microvascular injury, even prior to clinical manifestations [18] [19]. Additionally, novel biomarkers such as endocan have been proposed as complementary indicators of endothelial activation; Vatansever *et al.* (2025) demonstrated correlations between serum endocan, sICAM-1, and MetS components [11]. Altogether, these findings support the hypothesis that elevated circulating adhesion molecules reflect early endothelial involvement in metabolic dysregulation. Our results, showing higher sICAM-1 and E-selectin in participants with 1 - 2 alterations and in those with MetS, are consistent with this pattern.

Sex-specific biology strongly influences the development and presentation of metabolic dysregulation, including endothelial dysfunction, inflammatory responses, and adipokine signaling. In our cohort, men showed more pronounced increases in sICAM-1, E-selectin, and leptin, whereas changes were less consistent in women. These observations align with evidence that sex hormones, sex-chromosome-linked gene expression, and body-fat distribution modulate vascular responses to metabolic stress [1]-[3] [20] [21]. Estrogen enhances endothelial nitric oxide synthase activity, reduces oxidative stress, suppresses NF-κB activation, and downregulates adhesion molecule expression, conferring vascular protection in premenopausal women [4] [19]. Conversely, androgens may exacerbate vascular inflammation and accelerate endothelial dysfunction in men [13] [20] [21]. Beyond hormonal influences, sex-specific immune and vascular responses are shaped by intrinsic genetic and cellular mechanisms, as reported by McClements *et al.* (2025) and Robert (2023) [20] [21]. Santos-Marcos *et al.* (2023) further described how

sex hormones modulate endothelial interactions under diet-induced dysbiosis, producing sex-dependent vascular inflammation and altered endothelial permeability [22]. Collectively, these data suggest that sex modulates both the timing and magnitude of endothelial and inflammatory alterations in MetS. Our findings of higher adhesion molecules in men support this evidence and underscore the importance of sex-specific biomarker interpretation.

Adipose tissue functions not only as an energy reservoir but also as a dynamic endocrine organ governing systemic metabolism, inflammation, and vascular homeostasis. The balance between pro- and anti-inflammatory adipokines determines the transition from healthy adipose expansion to metabolic dysfunction [1] [3] [4]. In our study, leptin was significantly elevated in men with MetS, while adiponectin showed a decreasing trend and resistin remained unchanged. This pattern reflects an early shift toward a pro-inflammatory adipokine phenotype, consistent with reports demonstrating that leptin promotes oxidative stress, endothelial activation, and vascular remodeling [23]-[26]. Reduced adiponectin impairs NO bioavailability, enhances inflammatory signaling, and has been associated with endothelial dysfunction and increased cardiometabolic risk [27] [28]. Resistin, derived from macrophages and pre-adipocytes, also contributes to vascular inflammation and stiffness [29]; the absence of differences in resistin in our cohort may indicate a very early stage before macrophage infiltration intensifies. Reviews emphasize that evaluating adipokine patterns, rather than individual molecules, provides a more accurate representation of early metabolic risk [30]. Our findings support this multidimensional model, suggesting that adipokine imbalance contributes to endothelial activation early in the course of metabolic deterioration.

From a clinical standpoint, early biomarkers should be evaluated not only through statistical differences but also through diagnostic performance. In our cohort, sICAM-1 and E-selectin showed high specificity and favorable PPV despite modest sensitivity, reflecting strong rule-in value for early metabolic alterations. The combined use of both biomarkers improved diagnostic accuracy, consistent with growing evidence that multi-marker strategies enhance early detection of cardiometabolic risk [24] [31]-[33]. These findings support the robustness of using adhesion molecules as early endothelial indicators, particularly in populations where metabolic disease is still subclinical.

This study has some limitations that should be considered when interpreting the findings. Its cross-sectional design does not allow the establishment of temporal or causal relationships; however, it provides a valuable snapshot of early endothelial and metabolic changes in a large cohort of young adults. The sample was drawn from a single university population, which may limit broad generalization, yet it offers a well-defined and homogeneous group ideal for detecting early alterations. Biomarkers were measured at a single time point, but this approach ensured standardized conditions for all participants. Additionally, inflammatory cytokines such as CRP, IL-6, and TNF-α were not assessed; incorporating these

markers in future research may help refine mechanistic interpretations. Despite these considerations, the study provides novel and relevant evidence of early endothelial activation associated with metabolic risk in young individuals.

In light of these limitations, our findings nevertheless identify sICAM-1 and E-selectin as practical candidates for early endothelial risk assessment in young adults. Future prospective studies should test sex-specific cut-offs, evaluate multi-biomarker panels, and define their integration into clinical and public-health screening programs.

From a practical standpoint, the assessment of sICAM-1 and E-selectin could complement existing metabolic screening strategies for young adults. These biomarkers can be measured with widely available ELISA-based methods, require only a single blood sample, and could be incorporated alongside routine assessments such as fasting glucose, lipid profiles, and waist circumference in university health services or primary-care settings. Their high specificity suggests that they may be particularly valuable for identifying individuals who warrant closer metabolic follow-up, despite having only mild or subclinical alterations. Integrating these markers into early screening initiatives could facilitate timely lifestyle interventions, and targeted prevention strategies before the onset of overt MetS.

5. Conclusions

This study shows that endothelial adhesion molecules sICAM-1 and E-selectin, are early, non-invasive biomarkers of endothelial dysfunction in young adults with initial metabolic alterations. Even in the absence of clinically defined MetS, elevated concentrations indicate early vascular activation, supporting the notion that endothelial stress precedes overt metabolic disease.

The high specificity and Positive Predictive Values (PPV) observed for both markers, and the incremental diagnostic performance when they are evaluated together, support their combined use within a multi-biomarker approach for early cardiometabolic screening, potentially strengthening preventive strategies by enabling earlier identification of at-risk individuals.

A sex-specific pattern emerged, with men showing earlier and more pronounced alterations in endothelial markers and adipokines. These differences highlight the need for sex-aware thresholds and tailored preventive strategies in future clinical applications.

In summary, the simultaneous assessment of sICAM-1 and E-selectin offers a promising and cost-effective tool, for the early detection of endothelial dysfunction and metabolic risk in apparently healthy young adults. Longitudinal studies are warranted to confirm predictive value, refine cut-offs (by sex), and define integration into clinical and public health screening programs.

Acknowledgements

Supported in part by grants PICDS08-69 from Instituto de Ciencia y Tecnología del Distrito Federal to RVM; PAPIIT-DGAPA, UNAM (IN221123, IN228826 to IAGO and IN228825 to RVM). To M. Murguía for technical assistance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Matheus, A.S.D.M., Tannus, L.R.M., Cobas, R.A., Palma, C.C.S., Negrato, C.A. and Gomes, M.D.B. (2013) Impact of Diabetes on Cardiovascular Disease: An Update. *International Journal of Hypertension*, **2013**, Article ID: 653789. https://doi.org/10.1155/2013/653789

[2] Pontiroli, A.E., Frigè, F., Paganelli, M. and Folli, F. (2008) In Morbid Obesity, Metabolic Abnormalities and Adhesion Molecules Correlate with Visceral Fat, Not with Subcutaneous Fat: Effect of Weight Loss through Surgery. *Obesity Surgery*, **19**, 745-750. https://doi.org/10.1007/s11695-008-9626-4

[3] Bays, H.E. (2009) "Sick Fat," Metabolic Disease, and Atherosclerosis. *The American Journal of Medicine*, **122**, S26-S37. https://doi.org/10.1016/j.amjmed.2008.10.015

[4] Tanti, J., Ceppo, F., Jager, J. and Berthou, F. (2013) Implication of Inflammatory Signaling Pathways in Obesity-Induced Insulin Resistance. *Frontiers in Endocrinology*, **3**, Article 181. https://doi.org/10.3389/fendo.2012.00181

[5] Gómez Rosso, L., Benítez, M.B., Fornari, M.C., Berardi, V., Lynch, S., Schreier, L., *et al.* (2008) Alterations in Cell Adhesion Molecules and Other Biomarkers of Cardiovascular Disease in Patients with Metabolic Syndrome. *Atherosclerosis*, **199**, 415-423. https://doi.org/10.1016/j.atherosclerosis.2007.11.007

[6] Benítez, M.B., Cuniberti, L., Fornari, M.C., Gómez Rosso, L., Berardi, V., Elikir, G., *et al.* (2008) Endothelial and Leukocyte Adhesion Molecules in Primary Hypertriglyceridemia. *Atherosclerosis*, **197**, 679-687. https://doi.org/10.1016/j.atherosclerosis.2007.04.005

[7] Jacobs, M., Van Greevenbroek, M.M.J., Van Der Kallen, C.J.H., Ferreira, I., Blaak, E.E., Feskens, E.J.M., *et al.* (2009) Low-Grade Inflammation Can Partly Explain the Association between the Metabolic Syndrome and Either Coronary Artery Disease or Severity of Peripheral Arterial Disease: The CODAM Study. *European Journal of Clinical Investigation*, **39**, 437-444. https://doi.org/10.1111/j.1365-2362.2009.02129.x

[8] World Medical Association (2013) Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA*, **310**, 2191-2194. https://doi.org/10.1001/jama.2013.281053

[9] Wang, X. and He, B. (2024) Endothelial Dysfunction: Molecular Mechanisms and Clinical Implications. *MedComm*, **5**, e651. https://doi.org/10.1002/mco2.651

[10] Kwaifa, I.K., Bahari, H., Yong, Y.K. and Noor, S.M. (2020) Endothelial Dysfunction in Obesity-Induced Inflammation: Molecular Mechanisms and Clinical Implications. *Biomolecules*, **10**, Article 291. https://doi.org/10.3390/biom10020291

[11] Vatansever, M., Yaman, S., Cimbek, A., Sezgin, Y. and Yaman, S.O. (2025) Serum Endocan Levels Correlate with Metabolic Syndrome Severity and Endothelial Dysfunction: A Cross-Sectional Study Using the Mets-Z Score. *Metabolites*, **15**, Article 521. https://doi.org/10.3390/metabo15080521

[12] Alberti, K.G.M.M., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A., *et al.* (2009) Harmonizing the Metabolic Syndrome. *Circulation*, **120**, 1640-1645. https://doi.org/10.1161/circulationaha.109.192644

[13] Jiménez-Flores, J.R., Murguía-Romero, M., Mendoza-Ramos, M.I., Sigrist-Flores, S., Rodríguez-Soriano, N.Y., Ramírez-García, L.I., *et al.* (2012) Metabolic Syndrome Oc-

currence in University Students from México City: The Binomium HDL/Waist Circumference Is the Major Prevalence Factor. *Open Journal of Preventive Medicine*, **2**, 177-182. https://doi.org/10.4236/ojpm.2012.22026

[14] Ray, A., Ch. Maharana, K., Meenakshi, S. and Singh, S. (2023) Endothelial Dysfunction and Its Relation in Different Disorders: Recent Update. *Health Sciences Review*, **7**, Article ID: 100084. https://doi.org/10.1016/j.hsr.2023.100084

[15] Scioli, M.G., Storti, G., D'Amico, F., Rodríguez Guzmán, R., Centofanti, F., Doldo, E., *et al.* (2020) Oxidative Stress and New Pathogenetic Mechanisms in Endothelial Dysfunction: Potential Diagnostic Biomarkers and Therapeutic Targets. *Journal of Clinical Medicine*, **9**, Article 1995. https://doi.org/10.3390/jcm9061995

[16] Mulhem, A., Moulla, Y., Klöting, N., Ebert, T., Tönjes, A., Fasshauer, M., *et al.* (2020) Circulating Cell Adhesion Molecules in Metabolically Healthy Obesity. *International Journal of Obesity*, **45**, 331-336. https://doi.org/10.1038/s41366-020-00667-4

[17] Kumari, J.A., Bhaskar, M.V., Sanober, A., Mohan, I.K., Sreedevi, N.N., Noorjahan, M., *et al.* (2024) Intercellular Adhesion Molecules as Novel Markers of Endothelial Function in Patients with Diabetes Mellitus in the South Indian Population. *Journal of Clinical and Scientific Research*, **13**, 274-279. https://doi.org/10.4103/jcsr.jcsr_201_23

[18] Patel, R.B., Colangelo, L.A., Reiner, A.P., Gross, M.D., Jacobs, D.R., Launer, L.J., *et al.* (2020) Cellular Adhesion Molecules in Young Adulthood and Cardiac Function in Later Life. *Journal of the American College of Cardiology*, **75**, 2156-2165. https://doi.org/10.1016/j.jacc.2020.02.060

[19] Siddiqui, K., George, T.P., Mujammami, M., Isnani, A. and Alfadda, A.A. (2023) The Association of Cell Adhesion Molecules and Selectins (VCAM-1, ICAM-1, E-Selectin, L-Selectin, and P-Selectin) with Microvascular Complications in Patients with Type 2 Diabetes: A Follow-Up Study. *Frontiers in Endocrinology*, **14**, Article 1072288. https://doi.org/10.3389/fendo.2023.1072288

[20] McClements, L., Kautzky-Willer, A., Kararigas, G., Ahmed, S.B. and Stallone, J.N. (2025) The Role of Sex Differences in Cardiovascular, Metabolic, and Immune Functions in Health and Disease: A Review for "Sex Differences in Health Awareness Day". *Biology of Sex Differences*, **16**, Article No. 33. https://doi.org/10.1186/s13293-025-00714-7

[21] Robert, J. (2023) Sex Differences in Vascular Endothelial Cells. *Atherosclerosis*, **384**, Article ID: 117278. https://doi.org/10.1016/j.atherosclerosis.2023.117278

[22] Santos-Marcos, J.A., Mora-Ortiz, M., Tena-Sempere, M., Lopez-Miranda, J. and Camargo, A. (2023) Interaction between Gut Microbiota and Sex Hormones and Their Relation to Sexual Dimorphism in Metabolic Diseases. *Biology of Sex Differences*, **14**, Article No. 4. https://doi.org/10.1186/s13293-023-00490-2

[23] Poetsch, M.S., Strano, A. and Guan, K. (2020) Role of Leptin in Cardiovascular Diseases. *Frontiers in Endocrinology*, **11**, Article 354. https://doi.org/10.3389/fendo.2020.00354

[24] Yan, Y., Wang, L., Zhong, N., Wen, D. and Liu, L. (2024) Multifaced Roles of Adipokines in Endothelial Cell Function. *Frontiers in Endocrinology*, **15**, Article 1490143. https://doi.org/10.3389/fendo.2024.1490143

[25] Vilariño-García, T., Polonio-González, M., Pérez-Pérez, A., Ribalta, J., Arrieta, F., Aguilar, M., *et al.* (2024) Role of Leptin in Obesity, Cardiovascular Disease, and Type 2 Diabetes. *International Journal of Molecular Sciences*, **25**, Article 2338. https://doi.org/10.3390/ijms25042338

[26] Becerril, S., Rodríguez, A., Catalán, V., Ramírez, B., Unamuno, X., Portincasa, P., *et*

al. (2019) Functional Relationship between Leptin and Nitric Oxide in Metabolism. *Nutrients*, **11**, Article 2129. https://doi.org/10.3390/nu11092129

[27] Wang, X., Chen, Q., Pu, H., Wei, Q., Duan, M., Zhang, C., *et al.* (2016) Adiponectin Improves NF-κB-Mediated Inflammation and Abates Atherosclerosis Progression in Apolipoprotein E-Deficient Mice. *Lipids in Health and Disease*, **15**, Article No. 33. https://doi.org/10.1186/s12944-016-0202-y

[28] Lee, S., Zhang, H., Chen, J., Dellsperger, K.C., Hill, M.A. and Zhang, C. (2012) Adiponectin Abates Diabetes-Induced Endothelial Dysfunction by Suppressing Oxidative Stress, Adhesion Molecules, and Inflammation in Type 2 Diabetic Mice. *American Journal of Physiology-Heart and Circulatory Physiology*, **303**, H106-H115. https://doi.org/10.1152/ajpheart.00110.2012

[29] Fargnoli, J.L., Sun, Q., Olenczuk, D., Qi, L., Zhu, Y., Hu, F.B., *et al.* (2010) Resistin Is Associated with Biomarkers of Inflammation While Total and High-Molecular Weight Adiponectin Are Associated with Biomarkers of Inflammation, Insulin Resistance, and Endothelial Function. *European Journal of Endocrinology*, **162**, 281-288. https://doi.org/10.1530/eje-09-0555

[30] Farkhondeh, T., Llorens, S., Pourbagher-Shahri, A.M., Ashrafizadeh, M., Talebi, M., Shakibaei, M., *et al.* (2020) An Overview of the Role of Adipokines in Cardiometabolic Diseases. *Molecules*, **25**, Article 5218. https://doi.org/10.3390/molecules25215218

[31] Mustafa, A.I., Ebrahim, A.A., Abel Halim, W.A.L., Fawzy, E. and Abdou, A.F. (2022) Serum Soluble Intercellular Adhesion Molecule-1 (sICAM-1). *Indian Journal of Dermatology*, **67**, 512-517. https://doi.org/10.4103/ijd.ijd_387_21

[32] Lee, C., Kuo, F., Tang, W., Lu, C., Su, S., Liu, J., *et al.* (2019) Serum E-Selectin Concentration Is Associated with Risk of Metabolic Syndrome in Females. *PLOS ONE*, **14**, e0222815. https://doi.org/10.1371/journal.pone.0222815

[33] Mellott, E. and Faulkner, J.L. (2022) Mechanisms of Leptin-Induced Endothelial Dysfunction. *Current Opinion in Nephrology & Hypertension*, **32**, 118-123. https://doi.org/10.1097/mnh.0000000000000867