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Serum Endocan Levels in Adult Asthma Patients: A Controlled Study Investigating Associations With Disease Severity and Asthma Control

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ABSTRACT

Objective: Asthma is a heterogeneous disease characterized by chronic airway inflammation and variable respiratory symptoms, including episodic dyspnea, cough, wheezing, and chest tightness. While airway inflammation is well established in asthma pathophysiology, data on endothelial dysfunction are limited. Endothelial cell-specific molecule-1 (Endocan), a proteoglycan released by endothelial cells in response to inflammatory stimuli, has recently emerged as a potential biomarker of endothelial injury. This study aimed to investigate serum Endocan levels in asthma patients to evaluate the presence of endothelial dysfunction and explore its relationship with disease severity and control.

Materials and Methods: Fifty asthma patients and 39 healthy controls were enrolled. Participants with systemic comorbidities or active infections were excluded. Asthma severity was classified according to Global Initiative for Asthma (GINA) 2019 criteria, and asthma control was assessed using the Asthma Control Test (ACT). Pulmonary function tests (PFTs) were performed in accordance with the American Thoracic Society (ATS)/European Respiratory Society (ERS) standards. Serum Endocan levels were measured. Statistical analyses were conducted using Student's t-test, Mann-Whitney U test, Chi-square test, and Spearman correlation analysis. A p-value <0.05 was considered statistically significant.

Results: The asthma and control groups did not differ in age, sex, BMI, or smoking status. While forced expiratory volume in one second (FEV_1) and FEV_1/forced vital capacity (FVC) ratios were significantly lower in asthma patients, serum Endocan levels were notably higher (p<0.001). However, Endocan levels did not differ significantly across asthma severity groups or between controlled and uncontrolled asthma. No significant correlations were observed between Endocan levels, ACT scores, or pulmonary function parameters.

Conclusion: Higher Endocan levels in asthma patients suggest that endothelial dysfunction may contribute to asthma pathophysiology. However, the lack of association with disease severity and control limits its potential as a monitoring biomarker. Further prospective studies are warranted.

Keywords: Asthma, endothelial dysfunction, endocan, biomarker

INTRODUCTION

Asthma is a heterogeneous disease characterized by chronic airway inflammation and presents with symptoms such as episodic shortness of breath, cough, wheezing, and chest tightness (1). In addition to airway inflammation, varying degrees of endothelial injury and microvascular inflammation are also observed in this condition (2).

While airway inflammation has long been recognized and extensively studied as a well-defined pathophysiological feature of asthma (3-5), data regarding endothelial dys-

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function remain limited (6-10). In recent years, endothelial cell-specific molecule-1 (Endocan) a proteoglycan derived from endothelial cells, has emerged as a potential biomarker, particularly in the processes of inflammation and endothelial dysfunction.

Endocan, primarily expressed in pulmonary and renal endothelial cells, is released in response to pro-inflammatory and angiogenic stimuli. By modulating adhesion molecules, it plays a role in preventing leukocyte adhesion to the endothelium, thereby contributing to immune regulation and the maintenance of vascular integrity (11,12).

Through these mechanisms, Endocan has attracted attention as a promising biomarker, particularly due to its high expression in pulmonary endothelium. The increasing interest in this molecule suggests its potential use in the diagnosis and monitoring of inflammatory and malignant diseases of the respiratory system (13). Understanding endothelial injury in asthma is particularly important because it may contribute not only to local airway pathology but also to systemic consequences such as increased cardiovascular risk, which is more frequently observed in patients with chronic respiratory diseases (8).

Despite this potential, clinical studies evaluating the role of Endocan in respiratory diseases remain limited. The existing literature suggests that serum Endocan levels may be associated with disease severity in conditions such as lung cancer, acute lung injury, acute respiratory distress syndrome (ARDS), community-acquired pneumonia, pulmonary embolism, and obstructive sleep apnea (14-19). However, the number of studies investigating Endocan levels specifically in patients with asthma is quite limited (20,21). Recent work by Koksal et al. has demonstrated that nasal Endocan levels were elevated in adolescents with allergic rhinitis, even in the absence of asthma, indicating upper airway endothelial damage potentially linked to oxidative stress (22). In parallel, Jia et al. have demonstrated that reduced DEL-1 expression in asthma patients leads to increased neutrophil adhesion and migration via the LFA-1/ICAM-1 pathway, implicating impaired endothelial regulation as a contributing mechanism in neutrophilic asthma (23).

Therefore, we aimed to evaluate the presence of endothelial dysfunction in asthma patients by measuring serum Endocan levels and to investigate the relationship of these levels with disease severity and asthma control in this study.

MATERIAL and METHODS

This study was conducted with the participation of 50 patients with asthma and 39 healthy individuals who presented to the outpatient clinic of the Department of Pulmonology at a tertiary university hospital. The inclusion criteria for the asthma group were being 18 years of age or older, having no known systemic comorbidities such as cardiovascular disease, neurological disorders, diabetes mellitus, renal or hepatic disease, or malignancy, and providing informed consent to participate in the study.

The control group consisted of individuals who presented to the same clinic during the same period, had no previous diagnosis of any respiratory disease, were 18 years of age or older, had no systemic comorbidities, and voluntarily agreed to participate in the study. The exclusion criteria, which were applied to both groups, included being under 18 years of age, having any respiratory disease other than asthma, having any of the aforementioned systemic diseases, exhibiting signs of an asthma exacerbation or active infection at the time of enrollment, and refusing to provide informed consent.

Age, sex, body mass index (BMI), and smoking history were recorded for all participants. Additionally for patients in the asthma group, information regarding their current medications and history of asthma exacerbations within the past year was obtained and documented.

Asthma patients were classified as having mild, moderate, or severe asthma based on the minimum level of treatment required to maintain control of symptoms and exacerbations. Patients whose asthma was controlled with step 1 and 2 treatments were classified as having mild asthma. This group included patients using only as-needed short-acting β2 agonists (SABA), low-dose inhaled corticosteroids (ICS), ICS/formoterol combinations, or leukotriene receptor antagonists (LTRA).

Patients whose asthma was controlled with step 3 treatment were classified as having moderate asthma. This group included those receiving a combination of low- or medium-dose ICS with long-acting β2 agonists (LABA) or low-dose ICS with LTRA. Patients requiring step 4 and 5 treatments to achieve control were classified as having severe asthma. This group included individuals receiving medium- or high-dose ICS in combination with LABA, tiotropium, or biological agents (1).

All patients were administered the Asthma Control Test (ACT), a five-item questionnaire that assesses daytime and nighttime symptoms, the need for rescue medication, and limitations in daily activities. The validated Turkish version of the ACT was used in this study (24,25). Patients with an ACT score of <20 were classified as having uncontrolled asthma, whereas those with a score of ≥20 were considered to have controlled asthma.

In addition, asthma patients were classified as having atopic or non-atopic asthma based on total IgE levels, findings suggestive of allergen sensitization (skin prick test results or clinical history), and the presence of comorbid atopic diseases (e.g., allergic rhinitis, atopic dermatitis). Patients with at least one of these features were considered to have atopic asthma. A total IgE level above 100 IU/mL was considered indicative of atopy in the absence of other clinical criteria. Serum Endocan levels were then compared between the atopic and non-atopic asthma subgroups.

All participants underwent pulmonary function testing (PFT). Measurements were performed using a Jaeger MasterScope® PC device in accordance with the American Thoracic Society (ATS)/European Respiratory Society (ERS) standards (26). Each measurement was repeated at least three times, and the best value was used for analysis. Spirometric evaluation included forced expiratory volume in one second (FEV_1, L and % predicted), forced vital capacity (FVC, L and % predicted), and the FEV_1/FVC ratio.

Serum Endocan levels were measured using a commercially available human ESM1 (Endothelial Cell Specific Molecule-1, Endocan) ELISA kit (FineTest, Wuhan Fine Biotech Co., Ltd.; Catalog No: EH0125). The assay is based on a double-antibody sandwich ELISA method, with a total assay time of approximately 4 hours. The detection range of the kit was 15.625-1000 pg/mL, and the sensitivity was 9.375 pg/mL.

Venous blood samples were collected from all participants during morning hours. The samples were centrifuged at 3000 rpm for 10 minutes at 4°C, and the obtained serum was aliquoted and stored at -80°C until analysis. All samples were tested in duplicate. Absorbance was measured at 450 nm using an ELx800 microplate reader. Concentrations were calculated based on standard curves generated using kit-provided standards, with R^2 values close to 1.0, indicating high assay validity. Systemic corticosteroids were not administered to any participants, as none were experiencing an asthma exacerbation at the time of enrollment. However, patients receiving maintenance treatment with biologic agents (e.g., anti-IL-5) were not excluded from the study.

In addition to Endocan measurement, hematological indices such as absolute neutrophil count, absolute eosinophil count, and neutrophil-to-lymphocyte ratio (NLR) were obtained from the complete blood count performed on the same day. These markers were included in the statistical analysis to assess potential correlations with serum Endocan levels, as they are commonly used indicators of systemic inflammation relevant to asthma phenotypes.

The study was designed as a prospective observational study and was approved by the Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 10.05.2018, Protocol No: 2018/1394). Written informed consent was obtained from all participants prior to enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statement on AI use: No generative artificial intelligence (AI) tools were used in the preparation, writing, or editing of this manuscript.

Statistical Analysis

Statistical analyses were performed using the SPSS statistical software package, version 21.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using visual inspection (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and as median (minimum-maximum) for non-normally distributed variables. The Chi-square test was used to compare categorical variables. For comparisons of continuous variables between independent groups, Student's t-test was used for normally distributed data, and the Mann-Whitney U test was applied for non-normally distributed data. Correlations of non-normally distributed continuous variables were evaluated using Spearman's correlation analysis. A p-value <0.05 was considered statistically significant.

RESULTS

In the asthma group, 78% of the 50 patients were female, and the mean age was 44.82 ± 14.53 years. In the control group, 66.7% of the 39 participants were female,

with a mean age of 47.56 ± 16.25 years. The groups did not differ significantly in gender distribution (p=0.232) or mean age (p=0.404). The mean body mass index (BMI) was 28.84 ± 6.04 in the asthma group and 27.82 ± 5.63 in the control group, with no significant difference between the groups (p=0.419).

Regarding smoking status, 18% of individuals in the asthma group were current smokers, 70% had never smoked, and 12% were former smokers. In the control group, the corresponding rates were 20.5%, 66.7%, and 12.8%, respectively. No significant difference was observed in smoking history between the groups (p=0.942). The median smoking amounts were 10 pack-years in the asthma group and 20 pack-years in the control group, with no statistically significant difference (p=0.501).

Pulmonary function test results showed that the median percentage of predicted forced vital capacity (FVC) was 100.5% in the asthma group and 101% in the control group (p=0.171). However, the percentage of predicted forced expiratory volume in one second (FEV_1) was significantly lower in the asthma group (85.52 ± 21.14) compared to the control group (98.87 ± 13.05) (p=0.001). Similarly, the FEV_1/FVC ratio was significantly reduced in the asthma group (75.38 ± 8.56) compared to the control group (80.56 ± 5.44) (p<0.001). Additionally, serum Endocan levels were significantly higher in the asthma group than in the control group (p<0.001). These findings are summarized in Table I.

According to the GINA 2019 criteria, 12% of the asthma patients were classified as having mild asthma, 72% as moderate, and 16% as severe. No significant differences were found among these groups in terms of age, sex, BMI, smoking history, or smoking amount (p=0.534, 0.720, 0.743, 0.658, and 0.491, respectively). ACT scores were 22 ± 1.89 in the mild asthma group, 20.41 ± 2.97 in the moderate group, and 13 ± 4.03 in the severe group, with significantly lower scores in the severe asthma group (p<0.001). There were no statistically significant differences among these groups regarding pulmonary function parameters and serum Endocan levels (p=0.527, 0.454, 0.460, and 0.063, respectively). These findings are presented in Table II.

When asthma patients were evaluated based on ACT scores, 29 (58%) were classified as having controlled asthma, while 21 (42%) were classified as uncontrolled. There were no statistically significant differences between these groups regarding age, sex, BMI, smoking history, or smoking amount (p=0.445, 0.166, 0.409, 0.069, and 0.585, respectively). Furthermore, no significant differences were observed between patients with controlled and uncontrolled asthma in terms of pulmonary function test parameters and serum Endocan levels (p=0.279, 0.165, 0.052, and 0.173, respectively). These data are shown in Table III.

Table I: Comparison of Sociodemographic Characteristics, Pulmonary Function Test Results, and Serum Endocan Levels Between Asthma and Control Groups

Variable	Asthma (n=50)	Control (n=39)	p-value
Age (years), mean ± SD	44.82±14.53	47.56±16.25	0.404
Sex, n (%) - Female - Male	 39 (78) 11 (22)	 26 (66.7) 13 (33.3)	0.232
Smoking status, n (%) - Current smoker - Never smoked - Former smoker	 9 (18) 35 (70) 6 (12)	 8 (20.51) 26 (66.66) 5 (12.82)	0.942
Smoking amount (pack-years), median (IQR)	10 (8-25)	20 (7.5-26.5)	0.501
FVC (% predicted), median (IQR)	100.5 (91.5-109.25)	101 (93-111)	0.381
FEV_1 (% predicted), mean ± SD	85.52 ± 21.14	100.43 ± 19.60	0.001
FEV_1 /FVC ratio, mean ± SD	75.38 ± 8.56	80.56 ± 5.44	0.001
Serum Endocan (pg/mL), mean ± SD	775.08 ± 262.22	108.19 ± 51.11	<0.001

SD: Standard deviation, **IQR**: Interquartile range, **FVC**: Forced vital capacity, **FEV_1**: Forced expiratory volume in 1 second.

p-values for Age, FEV_1, FEV_1/FVC, and Serum Endocan: Independent samples t-test. p-values for Smoking amount and FVC: Mann-Whitney U test. p-values for categorical variables: Chi-square test.

Table II: Comparison of Sociodemographic Characteristics, Pulmonary Function Test Findings, and Serum Endocan Levels in Patients Classified by Asthma Severity

Variable	Mild Asthma (n=6)	Moderate Asthma (n=36)	Severe Asthma (n=8)	p-value
Age (years), mean ± SD	39.83 ± 15.38	44.77 ± 15.61	48.75 ± 7.22	0.534
Sex, n (%) - Female - Male	 5 (83.33) 1 (16.67)	 28 (77.77) 8 (22.23)	 6 (75) 2 (25)	 0.720
BMI, mean ± SD	27.5 ± 5.2	29.25 ± 6.26	28 ± 6.11	0.743
Smoking status, n (%) - Current smoker - Never smoked - Former smoker	 1 (16.67) 4 (66.66) 1 (16.67)	 5 (13.88) 27 (75) 4 (11.12)	 3 (37.50) 4 (50) 1 (12.50)	 0.658
Smoking amount (pack-years), median (IQR)	21 (5-27)	10 (6-12.5)	22.5 (12.5-25)	0.491
ACT score, mean ± SD	22 ± 1.89	20.41 ± 2.97	13 ± 4.03	<0.001*
FVC (% predicted), median (IQR)	99.5 (92-110)	102 (94-109.75)	92.5 (72.75-114)	0.527
FEV_1 (% predicted), mean ± SD	85.83 ± 20.31	87.38 ± 20.50	76.87 ± 25.09	0.454
FEV_1/FVC ratio, mean ± SD	76.16 ± 12.17	76.02 ± 8.20	71.87 ± 6.85	0.460
Serum Endocan (pg/mL), mean ± SD	992.43 ± 123.73	761.64 ± 270.22	672.52 ± 227.67	0.063

SD: Standard deviation, **IQR**: Interquartile range, **BMI**: Body mass index, **FVC**: Forced vital capacity, **FEV_1**: Forced expiratory volume in 1 second, **ACT**: Asthma Control Test.

p-values were calculated using one-way ANOVA (for normally distributed variables), Kruskal-Wallis test (for non-normally distributed variables), and Chi-square test (for categorical variables).

Table III: Comparison of Sociodemographic Characteristics, Pulmonary Function Test Findings, and Serum Endocan Levels in Patients Classified by Asthma Control Status

Variable	Controlled Asthma (n=29)	Uncontrolled Asthma (n=21)	p-value
Age (years), mean ± SD	46.17 ± 16.12	42.95 ± 12.13	0.445
Sex, n (%) - Female - Male	25 (86.2) 4 (13.79)	14 (66.66) 7 (33.33)	0.166
BMI, mean ± SD	29.44 ± 5.77	28 ± 6.45	0.409
Smoking status, n (%) - Current smoker - Never smoked - Former smoker	 3 (10.34) 24 (82.75) 2 (6.89)	 6 (28.57) 11 (52.38) 4 (19.04)	0.069
Smoking amount (pack-years), median (IQR)	10 (4-37)	10 (9.5-21.25)	0.585
ACT score, mean ± SD	22.24 ± 1.55	15.52 ± 3.38	<0.001*
FVC (% predicted), median (IQR)	102 (94-113.5)	97 (85.5-106.5)	0.279
FEV_1 (% predicted), mean ± SD	89.09 ± 19.74	80.61 ± 22.50	0.165
FEV_1/FVC ratio, mean ± SD	77.37 ± 8.96	72.61 ± 7.31	0.052
Serum Endocan (pg/mL), mean ± SD	818.36 ± 268.47	715.30 ± 247.15	0.173

SD: Standard deviation, **IQR**: Interquartile range, **BMI**: Body mass index, **FVC**: Forced vital capacity, **FEV_1**: Forced expiratory volume in 1 second, **ACT**: Asthma Control Test.

p-values for Age, ACT score, FEV_1, FEV_1/FVC, and Serum Endocan: Independent samples t-test. p-values for Smoking amount and FVC: Mann-Whitney U test. p-values for categorical variables (Sex, Smoking status): Chi-square test.

Table IV: Correlation Analysis Between Serum Endocan Levels and Clinical and Pulmonary Function Parameters

Parameter	r	p-value
Age	0.000	0.999
BMI	-0.254	0.075
Smoking (pack-years)	-0.176	0.529
ACT score	0.265	0.063
FVC (% predicted)	0.139	0.336
FEV_1 (% predicted)	0.210	0.143
FEV_1/FVC ratio	0.253	0.077

r: Spearman's correlation coefficient, **BMI**: Body mass index, **FVC**: Forced vital capacity, **FEV_1**: Forced expiratory volume in 1 second, **ACT**: Asthma Control Test.

p-values were calculated using Spearman's correlation analysis.

In addition, no statistically significant difference in serum Endocan levels was observed between patients with atopic and non-atopic asthma (p = 0.84).

Finally, serum Endocan levels were not significantly correlated with age, BMI, smoking amount (pack-years), ACT scores, or pulmonary function test parameters (p>0.05). These correlations are summarized in Table IV.

There was also no statistically significant correlation between serum Endocan levels and neutrophil count (r = 0.034, p = 0.821), eosinophil count (r = -0.121, p = 0.429), or neutrophil-to-lymphocyte ratio (NLR) (r = 0.157, p = 0.298).

DISCUSSION

In this study, the relationship between serum Endocan levels and disease severity, asthma control status, and pulmonary function parameters was investigated in patients with asthma, and the findings were compared with those of healthy individuals. The significantly higher serum Endocan levels observed in the asthma group suggest a potential role of endothelial dysfunction in the pathophysiology of asthma.

The homogeneity of the asthma and control groups in terms of age, sex, body mass index (BMI), and smoking history, along with the exclusion of individuals with cardiovascular, neurological, metabolic, and malignant diseases, enhances the reliability of the results obtained in this study.

Similarly, previous research in patients with stable chronic obstructive pulmonary disease (COPD) demonstrated elevated Endocan levels compared to healthy controls, suggesting that endothelial dysfunction may be a common feature in chronic inflammatory airway diseases (27).

In the study by İn et al., Endocan levels were also found to correlate positively with disease severity, exacerbation frequency, and systolic pulmonary artery pressure, while inversely correlating with oxygen saturation (28).These findings underscore the clinical relevance of Endocan not only as a marker of inflammation but also as an indicator of vascular impairment in chronic airway diseases. Therefore, elevated Endocan levels observed in asthma patients in our study may reflect a shared pathophysiological pathway involving pulmonary endothelial activation and vascular remodeling.

However, studies evaluating Endocan levels specifically in asthma patients remain limited. In a study conducted in the pediatric population, serum Endocan levels were found to be higher compared to healthy controls and showed a negative correlation with FEV_1 and peak expiratory flow (PEF) (20). In contrast, Tsilogianni et al. evaluated serum and sputum Endocan levels in adult asthma patients across different severities and reported no significant association with disease severity (21). Notably, their study did not include a control group. To date, Tsilogianni et al.'s study appears to be the only investigation focusing on Endocan levels in adult asthma patients. Thus, the current evidence remains scarce and fragmented, underscoring the importance of our findings. By including a healthy control group, our study enabled a clearer comparative analysis and demonstrated significantly higher serum Endocan levels in asthma patients, supporting the hypothesis that endothelial dysfunction may be associated with the presence of asthma.

However, Endocan levels did not show significant differences when asthma patients were classified according to disease severity (mild, moderate, severe) or asthma control status (controlled vs. uncontrolled). This suggests that while Endocan may reflect the presence of asthma, it may not be sufficient to distinguish between different levels of disease severity or control.

Furthermore, when patients were classified based on atopic features (such as total IgE levels, allergen sensitization, and comorbid atopic diseases), serum Endocan levels did not significantly differ between atopic and non-atopic asthma subgroups. This finding suggests that Endocan may reflect an aspect of endothelial dysfunction that is independent of Th2-mediated inflammation. This perspective is supported by a recent umbrella review of meta-analyses evaluating Endocan across a wide range of diseases, which concluded that Endocan is a robust and consistent marker of vascular inflammation and cytokine-mediated endothelial injury in both infectious and non-infectious conditions (29). Its regulation by proinflammatory and angiogenic stimuli such as TNF-α and VEGF, and not by classical Th2 cytokines, strengthens its value as a Th2-independent endothelial biomarker.

This observation aligns with previous reports showing that Endocan expression is primarily induced by proinflammatory and angiogenic cytokines such as TNF-α, IL-1β, and VEGF, whereas classical Th2 cytokines like IL-4 have no significant effect (30). Therefore, Endocan may represent a marker of endothelial dysfunction rather than Th2-driven allergic inflammation.

While Tsilogianni et al. also reported no association between Endocan levels and asthma severity, their study did not explore the phenotypic characteristics of asthma, such as atopic status (21). Therefore, our findings provide novel insight by addressing this gap and highlighting the potential Th2-independent nature of Endocan elevation in asthma.

Furthermore, no significant correlation was found between Endocan levels and routine systemic inflammatory markers such as neutrophil and eosinophil counts or NLR. This finding suggests that Endocan may not be a general marker of systemic inflammation, but rather a specific indicator of local endothelial dysfunction (12,21,30). This aligns with previous literature emphasizing the endothelial origin and local activity of Endocan, particularly in pulmonary vascular inflammation.

Currently, there is no universally established reference range or diagnostic threshold for serum Endocan levels. Reported values in healthy individuals generally range between 250-500 pg/mL, depending on the study population and assay method used (12, 21). In our study, the mean serum Endocan level in asthma patients was 775.08 ± 262.22 pg/mL, which was significantly higher than that of the control group (108.19 ± 51.11 pg/mL, $p < 0.001$). This marked elevation suggests that Endocan may reflect subclinical endothelial dysfunction in asthma, even during stable disease periods.

Notably, the ELISA kit used in our study had a detection range of 15.625-1000 pg/mL and a sensitivity of 9.375 pg/mL, which may partially explain the higher observed values compared to studies using different assay platforms. However, due to the lack of standardized reference intervals or disease-specific cut-offs, the clinical utility of Endocan remains exploratory. Further large-scale prospective studies are needed to establish validated thresholds and to assess its diagnostic and prognostic implications in asthma and other inflammatory airway diseases.

Similarly, the lack of a significant correlation between Endocan levels and pulmonary function test parameters or ACT scores implies that this biomarker may be more indicative of endothelial inflammation rather than functional respiratory status.

Nevertheless, the relatively small number of patients, particularly in the mild and severe asthma subgroups, may have contributed to the absence of statistically significant differences in these analyses. Therefore, larger-scale, prospective studies are needed to better elucidate the relationship between Endocan levels and asthma severity. Moreover, future research should focus on serial measurements of Endocan levels, including assessments during exacerbation periods and after the initiation of biologic therapies, to evaluate its responsiveness to disease activity and treatment. Additionally, combining Endocan with other pro-angiogenic and endothelial markers such as vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) may enhance its prognostic and pathophysiological value in asthma.

This study has several limitations that should be acknowledged. First, it was conducted at a single center, which may limit the generalizability of the findings. Second, the moderate sample size may reduce the statistical power to detect more subtle associations. Third, due to the cross-sectional design, causal relationships between serum Endocan levels and asthma control or severity cannot be established. Additionally, only a single endothelial marker was measured, limiting the scope of vascular assessment. The absence of a broader panel of endothelial or angiogenic

biomarkers such as ICAM-1, VCAM-1, or VEGF restricts the mechanistic interpretation of endothelial dysfunction in asthma. Future longitudinal studies with larger, multicenter cohorts and a comprehensive biomarker panel are needed to better understand the temporal dynamics and mechanistic pathways of endothelial injury in asthma.

CONCLUSION

In this study, the significantly higher serum Endocan levels observed in asthma patients compared to healthy individuals support the potential role of endothelial dysfunction in the pathophysiology of asthma. However, the lack of association between Endocan levels and disease severity or asthma control status suggests that its value as a biomarker for disease monitoring or prognostication remains uncertain. Further large-scale, prospective, and multicenter studies, particularly those including serial measurements and evaluations during exacerbation periods, are needed to more clearly elucidate the relationship between Endocan levels and asthma progression and to determine its potential clinical utility.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Previous Presentation

This study has not been previously presented or published.

Author Contributions

Concept: **Aydın Col, Onur Yazici,** Design: **Aydın Col, Onur Yazici,** Data collection or processing: **Aydın Col, Cigdem Yenisey,** Analysis or Interpretation: **Onur Yazici,** Literature search: **Aydın Col, Onur Yazici, Cigdem Yenisey,** Writing: **Aydın Col, Onur Yazici, Cigdem Yenisey,** Approval: **Aydın Col, Onur Yazici, Cigdem Yenisey.**

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