



Metabolic dysfunction is associated with non-eosinophilic asthma phenotype: a retrospective cross-sectional study

Elif Fatma Özkan Pehlivanoglu , Ülker İrem İlhan , Furkan Güney , Yasemin Sağlan , Hüseyin Balcioğlu , Uğur Bilge* 

Faculty of Medicine, Department of Family Medicine, Eskişehir Osmangazi University, Eskişehir 26040, Turkey

***Correspondence:** Uğur Bilge, Faculty of Medicine, Department of Family Medicine, Eskişehir Osmangazi University, Eskişehir 26040, Turkey. dr_ubilge@windowslive.com

Academic Editor: Manlio Milanese, Struttura Complessa di Pneumologia Azienda Sociosanitaria Ligure 2, Italy

Received: June 24, 2026 **Accepted:** August 19, 2026 **Published:** October 9, 2026

Cite this article: Özkan Pehlivanoglu EF, İlhan Üİ, Güney F, Sağlan Y, Balcioğlu H, Bilge U. Metabolic dysfunction is associated with non-eosinophilic asthma phenotype: a retrospective cross-sectional study. *Explor Asthma Allergy*. 2026;4:1009136. <https://doi.org/10.37349/ea.2026.1009136>

Abstract

Aim: Asthma is a heterogeneous airway disease comprising distinct inflammatory phenotypes with variable clinical characteristics and treatment responses. Increasing evidence suggests that obesity-related metabolic dysfunction contributes to asthma pathogenesis; however, its relationship with eosinophilic asthma remains incompletely understood. This study aimed to evaluate metabolic dysfunction in patients with asthma and investigate its association with the eosinophilic phenotype using multiple insulin resistance-related metabolic indices.

Methods: In this retrospective cross-sectional study, 90 patients with asthma and 131 healthy controls were included. Metabolic dysfunction was assessed using body mass index (BMI), homeostatic model assessment for insulin resistance (HOMA-IR), triglyceride-glucose (TyG) index, cholesterol-glucose (CHG) index, and metabolic score for insulin resistance (METS-IR). Eosinophilic asthma was defined as a peripheral blood eosinophil count ≥ 300 cells/ μ L. Group comparisons and multivariable logistic regression analyses were performed to identify factors associated with eosinophilic asthma.

Results: Compared with healthy controls, patients with asthma demonstrated significantly higher BMI, HOMA-IR, METS-IR, peripheral eosinophil counts, and neutrophil-to-lymphocyte ratio (NLR), indicating greater metabolic dysfunction and systemic inflammation. Among patients with asthma, 27.8% were classified as having eosinophilic asthma. Patients with eosinophilic asthma had significantly lower BMI and METS-IR values than those with non-eosinophilic asthma. In the multivariable logistic regression analysis, METS-IR showed an inverse but non-significant association with eosinophilic asthma after adjustment for age, sex, inhaled corticosteroid (ICS) use, and NLR.

Conclusions: Metabolic dysfunction was more prevalent in patients with asthma than in healthy individuals. Although eosinophilic asthma was associated with lower BMI and METS-IR values in univariate analyses, these associations were not confirmed after adjustment for potential confounders. These findings suggest that metabolic dysfunction may contribute to asthma phenotypic heterogeneity and warrant confirmation in larger prospective studies.



Keywords

asthma, eosinophilic asthma, obesity, insulin resistance, METS-IR, metabolic dysfunction

Introduction

Asthma is a chronic heterogeneous airway disease characterized by variable respiratory symptoms, airway inflammation, and reversible airflow limitation [1]. Despite major advances in asthma management, substantial heterogeneity exists regarding inflammatory pathways, clinical manifestations, disease severity, and therapeutic responsiveness. Among the recognized inflammatory phenotypes, eosinophilic asthma has received particular attention because of its association with severe exacerbations, impaired disease control, and eligibility for targeted biologic therapies [2–4].

In recent years, obesity has emerged as one of the most important modifiable risk factors for both asthma development and progression. Epidemiological and mechanistic studies have demonstrated that obesity is associated with increased asthma prevalence, poorer symptom control, greater healthcare utilization, and reduced responsiveness to inhaled corticosteroids (ICSs) [5–7]. Importantly, obesity-related asthma is increasingly recognized as a distinct phenotype characterized by systemic inflammation, metabolic dysregulation, and non-type 2 immune responses rather than classical eosinophilic airway inflammation. Recent evidence suggests that metabolic abnormalities may influence asthma phenotypes through pathways involving adipokine imbalance, oxidative stress, insulin resistance, mitochondrial dysfunction, and chronic low-grade inflammation [5–9].

Although body mass index (BMI) remains the most widely used measure of obesity, it does not adequately capture metabolic health or visceral adiposity [10]. Consequently, several metabolic indices have been developed to provide a more comprehensive assessment of insulin resistance and cardiometabolic dysfunction. Among these, homeostatic model assessment for insulin resistance (HOMA-IR), triglyceride-glucose (TyG) index, cholesterol-glucose (CHG) and metabolic score for insulin resistance (METS-IR) have demonstrated strong associations with metabolic syndrome, cardiovascular disease, and chronic inflammatory disorders [11–14]. However, unlike the other indices, HOMA-IR requires measurement of fasting insulin levels, which may not be routinely available in many clinical settings, particularly in preventive health services, primary care, rural healthcare facilities, and resource-limited environments. In contrast, TyG, CHG, and METS-IR rely on routinely obtained clinical and biochemical parameters, making them more practical and accessible tools for large-scale screening and risk assessment. Evaluating the ability of these readily available indices to characterize asthma phenotypes may therefore enhance their clinical utility and improve risk stratification in everyday practice. Emerging evidence further suggests that metabolic dysfunction contributes not only to asthma susceptibility but also to disease severity and phenotypic heterogeneity [8].

Nevertheless, data evaluating the relationship between metabolic dysfunction and eosinophilic asthma remain limited. Most previous studies have focused on obesity as an isolated risk factor without simultaneously examining multiple metabolic indices that may better reflect the biological consequences of excess adiposity. Understanding whether metabolic burden differs between eosinophilic and non-eosinophilic asthma phenotypes may provide valuable insights into disease mechanisms and identify potential therapeutic targets.

Therefore, the present study aimed to evaluate metabolic dysfunction using multiple insulin resistance-related indices in patients with asthma and to investigate their association with the eosinophilic asthma phenotype.

Research hypotheses:

Hypothesis 1. Patients with asthma exhibit greater metabolic dysfunction, as assessed by BMI, HOMA-IR, TyG, CHG, and METS-IR, compared with healthy controls.

Hypothesis 2. Greater metabolic dysfunction is associated with a lower likelihood of the eosinophilic asthma phenotype.

Materials and methods

Study design and population

This is a retrospective cross-sectional study. The study included 90 patients diagnosed with Asthma and 131 healthy controls who attended the Family Medicine outpatient clinics between January 2018 and January 2025. Asthma diagnosis was confirmed according to the Global Initiative for Asthma (GINA) criteria based on compatible clinical symptoms and objective evidence of variable expiratory airflow limitation documented in medical records.

The control participants were not individually or frequency matched to patients with asthma according to age, sex, or smoking status. Potential differences in these variables were assessed statistically and, where appropriate, considered in adjusted analyses.

The control group consisted of individuals without a known history of asthma, chronic pulmonary disease, active infection, inflammatory disease, malignancy, or systemic corticosteroid use. Patients with incomplete medical records, pregnancy, hematological disorders, chronic inflammatory diseases, malignancy, chronic liver or kidney disease, and acute infectious conditions were excluded from the study. Potential confounding by corticosteroid therapy was addressed by excluding participants receiving systemic corticosteroids. ICS use was recorded, analyzed in a predefined subgroup analysis, and included as an adjustment variable in multivariable logistic regression analyses.

Classification of eosinophilic phenotype

Patients with asthma were classified according to peripheral blood eosinophil counts. Eosinophilic asthma was defined as a blood eosinophil count ≥ 300 cells/ μ L, based on commonly used thresholds in asthma phenotyping and biologic eligibility criteria. This threshold was selected because it is commonly used in asthma phenotyping studies and biologic therapy trials and provides relatively high specificity for clinically relevant eosinophilic inflammation. The eosinophil count closest to the index clinical assessment was used.

Data collection

Demographic and clinical data were extracted from electronic medical records, including age, sex, smoking status, body weight, height, and BMI. Laboratory parameters included fasting plasma glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting insulin, complete blood count parameters, and peripheral eosinophil counts. Additional subgroup analyses were performed according to ICS use.

BMI was calculated as body weight (kg) divided by height squared (m^2).

Metabolic indices

Metabolic indices reflecting insulin resistance and metabolic dysfunction were calculated using the following formulas:

$TyG = \ln[\text{fasting triglyceride (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$ [11];

$CHG = \ln\{[\text{total cholesterol (mg/dL)} \times \text{fasting glucose (mg/dL)}] / [2 \times \text{HDL-C (mg/dL)}]\}$ [12];

$HOMA-IR = \text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mg/dL)} / 405$ [13];

$METS-IR = \ln[(2 \times \text{fasting glucose}) + \text{triglyceride}] \times \text{BMI} / \ln(\text{HDL-C})$ [14].

Statistical analysis

Statistical analyses were performed using SPSS 22.0. The normality of continuous variables was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk test.

Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), depending on data distribution. Categorical variables were presented as frequencies and percentages.

Comparisons between two groups were performed using the independent samples *t*-test for normally distributed variables and the Mann-Whitney *U* test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test.

Multivariable logistic regression analysis was used to identify independent predictors of eosinophilic asthma. A *p*-value < 0.05 was considered statistically significant.

Because of the retrospective design, the sample size was determined by the number of eligible participants with complete data during the study period. A sensitivity power analysis was therefore performed for the available sample. At a two-sided alpha level of 0.05 and 80% power, the comparison between 90 patients with asthma and 131 controls was capable of detecting a standardized effect size of approximately 0.39.

Assessment of multicollinearity

Before constructing the multivariable logistic regression model, multicollinearity among the independent variables was assessed using variance inflation factors (VIFs) and tolerance statistics. Variables with VIF values > 5 (or > 10) and tolerance values < 0.20 were considered indicative of problematic multicollinearity. Because BMI is incorporated into the METS-IR formula and the metabolic indices share common biological components, multicollinearity was specifically evaluated before model construction. The final regression model was specified to minimize collinearity and improve the stability and interpretability of the regression estimates.

Results

A total of 221 participants were included in the study, comprising 90 patients with asthma and 131 healthy controls. The mean age was significantly higher in the asthma group compared with the control group (54.27 ± 15.93 vs. 49.63 ± 14.10 years, $p = 0.027$) (Table 1).

Table 1. Baseline characteristics of healthy controls and asthma subgroups.

Variable	Healthy controls (<i>n</i> = 131)	Non-eosinophilic asthma (<i>n</i> = 65)	Eosinophilic asthma (<i>n</i> = 25)	<i>p</i> -value
Age (years)	49.63 $\pm$ 14.10	54.49 $\pm$ 15.81	53.68 $\pm$ 16.54	0.039
Female, <i>n</i> (%)	95 (72.5)	47 (72.3)	17 (68.0)	0.923
Male, <i>n</i> (%)	36 (27.5)	18 (27.7)	8 (32.0)	-
BMI (kg/m ²)	26.78 $\pm$ 5.07	28.73 $\pm$ 4.73	27.60 $\pm$ 5.07	0.028
BMI category, <i>n</i> (%)				0.046
Normal	49 (37.4)	14 (21.5)	11 (44.0)	
Overweight	51 (38.9)	29 (44.6)	7 (28.0)	
Obese	31 (23.7)	22 (33.8)	7 (28.0)	
Glucose (mg/dL)	92.6 $\pm$ 19.2	96.8 $\pm$ 20.9	95.4 $\pm$ 18.5	0.312
Total cholesterol (mg/dL)	199.8 $\pm$ 37.9	196.7 $\pm$ 35.8	201.6 $\pm$ 39.2	0.761
Triglycerides (mg/dL)	123.4 (82.0–176.0)	128.0 (86.0–177.0)	131.0 (93.0–189.0)	0.418
LDL-C (mg/dL)	129.8 $\pm$ 35.2	127.6 $\pm$ 34.7	132.5 $\pm$ 37.1	0.684
HDL-C (mg/dL)	56.3 $\pm$ 14.7	53.9 $\pm$ 13.6	52.8 $\pm$ 12.8	0.271
Insulin (μ U/mL)	10.4 (6.7–15.9)	11.8 (7.9–17.6)	13.4 (8.8–18.3)	0.084
HOMA-IR	2.1 (1.3–3.2)	2.5 (1.6–3.8)	2.8 (1.8–4.2)	0.071
HbA1c (%)	5.47 $\pm$ 0.63	5.53 $\pm$ 0.59	5.56 $\pm$ 0.62	0.612
Hemoglobin (g/dL)	13.4 $\pm$ 1.5	13.5 $\pm$ 1.6	13.7 $\pm$ 1.7	0.593
Hematocrit (%)	40.0 $\pm$ 4.2	40.4 $\pm$ 4.4	40.8 $\pm$ 4.7	0.547
Erythrocyte ($\times 10^6/\mu$ L)	4.63 $\pm$ 0.46	4.71 $\pm$ 0.52	4.78 $\pm$ 0.55	0.421

Table 1. Baseline characteristics of healthy controls and asthma subgroups. (continued)

Variable	Healthy controls (n = 131)	Non-eosinophilic asthma (n = 65)	Eosinophilic asthma (n = 25)	p-value
MCV (fL)	85.8 ± 6.3	84.7 ± 7.2	85.2 ± 6.9	0.638
MCHC (g/dL)	33.3 ± 1.4	33.4 ± 1.5	33.2 ± 1.7	0.812
RDW (%)	14.1 ± 2.0	13.9 ± 1.8	14.2 ± 2.1	0.697
Leukocyte (× 10 ³ /μL)	6.9 ± 1.9	7.3 ± 2.1	7.6 ± 2.4	0.214
Neutrophil (× 10 ³ /μL)	4.0 ± 1.6	4.3 ± 1.8	4.5 ± 1.9	0.286
Lymphocyte (× 10 ³ /μL)	2.2 ± 0.7	2.3 ± 0.8	2.2 ± 0.7	0.731
Monocyte (× 10 ³ /μL)	0.47 ± 0.16	0.50 ± 0.18	0.54 ± 0.19	0.188
Eosinophil (× 10 ³ /μL)	0.15 (0.08–0.22)	0.11 (0.05–0.18)	0.55 (0.37–1.00)	< 0.001
Basophil (× 10 ³ /μL)	0.04 (0.02–0.07)	0.04 (0.02–0.07)	0.05 (0.03–0.08)	0.458
Platelet (× 10 ³ /μL)	257 ± 63	268 ± 71	281 ± 76	0.192

Data are presented as mean ± standard deviation, median (interquartile range), or *n* (%), as appropriate. Continuous variables were compared using one-way ANOVA or the Kruskal-Wallis test according to data distribution, and categorical variables were compared using the chi-square test or Fisher's exact test. BMI: body mass index; HbA1c: glycated hemoglobin; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostatic model assessment for insulin resistance; LDL-C: low-density lipoprotein cholesterol; MCHC: mean corpuscular hemoglobin concentration; MCV: mean corpuscular volume; RDW: red cell distribution width.

Laboratory comparisons demonstrated significantly higher peripheral eosinophil counts in patients with asthma compared with controls (190 vs. 105 cells/μL, *p* = 0.029). The neutrophil-to-lymphocyte ratio (NLR) was also modestly but significantly elevated in the asthma group (*p* = 0.037), suggesting increased systemic inflammatory burden. Regarding metabolic parameters, HOMA-IR and METS-IR were significantly higher in patients with asthma than in controls (both *p* < 0.001), indicating increased insulin resistance and metabolic dysfunction (Table 2).

Table 2. Laboratory parameters and metabolic indices.

Variable	Asthma	Control	p-value
Eosinophil (cells/μL)	190 (100–310)	105 (60–210)	0.029
NLR	1.91 (1.46–2.47)	1.76 (1.34–2.25)	0.037
HOMA-IR	2.84 (2.01–4.17)	2.21 (1.63–3.01)	< 0.001
TyG index	8.71 (8.28–9.12)	8.54 (8.18–8.95)	0.084
METS-IR	44.74 (38.29–51.12)	38.89 (34.12–44.55)	< 0.001
CHG index	5.24 (4.98–5.58)	5.16 (4.92–5.39)	0.071

Data are presented as median (interquartile range). Comparisons between groups were performed using the Mann-Whitney *U* test. CHG: cholesterol-glucose; HOMA-IR: homeostatic model assessment for insulin resistance; METS-IR: metabolic score for insulin resistance; NLR: neutrophil-to-lymphocyte ratio; TyG: triglyceride-glucose.

Patients receiving ICS-containing therapies had significantly lower TyG, METS-IR, and CHG indices compared with non-ICS users (all *p* < 0.05). These findings may suggest a lower metabolic burden among ICS users or reflect differences in disease phenotype and treatment patterns (Table 3).

Table 3. Asthma subgroup according to ICS use.

Variable	ICS users	Non-ICS	p-value
Eosinophil (cells/μL)	198 (112–320)	170 (100–290)	0.412
HOMA-IR	2.73 (2.08–3.44)	2.92 (1.96–4.88)	0.287
TyG index	8.39 (8.11–8.91)	8.78 (8.51–9.20)	0.029
Metabolic score for insulin resistance	41.82 (37.20–48.73)	46.12 (40.53–52.20)	0.046
CHG index	5.08 (4.92–5.39)	5.31 (5.01–5.63)	0.031

Data are presented as median (interquartile range). Mann-Whitney *U* test was used. ICS-containing therapies included budesonide, fluticasone, beclomethasone, and fixed-dose ICS combinations. CHG: cholesterol-glucose; HOMA-IR: homeostatic model assessment for insulin resistance; ICS: inhaled corticosteroid; TyG: triglyceride-glucose.

Asthma patients were stratified according to predefined peripheral blood eosinophil thresholds. Using cutoffs of ≥ 150 and ≥ 300 , eosinophilic phenotype prevalence was 58.9% and 27.8%. Based on the predefined primary threshold of ≥ 300 cells/ μL , 25 patients were classified as having eosinophilic asthma (Table 4).

Table 4. Prevalence of eosinophilic phenotype.

Cutoff	Asthma <i>n</i> (%)
≥ 150 cells/ μL	53 (58.9)
≥ 300 cells/ μL	25 (27.8)

Data are presented as frequency and percentage. Eosinophilic phenotype was defined using absolute peripheral blood eosinophil counts with thresholds of ≥ 150 and ≥ 300 , based on previously published asthma phenotyping studies and biologic eligibility criteria.

Patients with eosinophilic asthma had significantly lower BMI compared with those with non-eosinophilic asthma (26.60 vs. 30.82 kg/ m^2 , $p = 0.023$). Similarly, METS-IR values were significantly lower in eosinophilic asthma patients (36.91 vs. 47.78, $p = 0.005$) (Table 5).

Table 5. Eosinophilic vs. non-eosinophilic asthma patients.

Variable	Eosinophilic (<i>n</i> = 25)	Non-eosinophilic (<i>n</i> = 65)	<i>p</i> -value
Age (years)	55 (41–64)	57 (46–66)	0.681
Female, <i>n</i> (%)	17 (68.0)	47 (72.3)	0.796
BMI (kg/ m^2)	26.60 (23.9–29.4)	30.82 (27.1–33.5)	0.023
Eosinophil (cells/ μL)	410 (310–700)	110 (90–200)	< 0.001
NLR	1.74 (1.43–2.34)	1.95 (1.62–2.51)	0.381
Homeostatic model assessment for insulin resistance	2.69 (2.11–3.29)	2.96 (2.00–5.12)	0.344
TyG index	8.53 (8.07–9.11)	8.74 (8.35–9.15)	0.467
Metabolic score for insulin resistance	36.91 (34.33–44.28)	47.78 (41.52–53.19)	0.005
CHG index	5.19 (4.92–5.47)	5.28 (4.99–5.62)	0.602
ICS use, <i>n</i> (%)	13 (52.0)	24 (36.9)	0.235

Data are presented as median (interquartile range) or *n* (%). Mann-Whitney *U* and Fisher's exact tests were used. BMI: body mass index; CHG: cholesterol-glucose; ICS: inhaled corticosteroid; NLR: neutrophil-to-lymphocyte ratio; TyG: triglyceride-glucose.

In the multivariable logistic regression analysis, including age, sex, ICS use, NLR, and METS-IR, none of the variables was independently associated with the eosinophilic asthma phenotype (Table 6). Although METS-IR demonstrated an inverse association with eosinophilic asthma [adjusted odds ratio (OR) 0.96, 95% CI 0.90–1.03], this association did not reach statistical significance ($p = 0.254$). No evidence of problematic multicollinearity was identified in the final model (Table 7).

Table 6. Multivariable logistic regression for eosinophilic asthma phenotype.

Predictor	Adjusted OR	95% CI	<i>p</i> -value
Age, per year	0.999	0.968–1.031	0.946
Female sex	0.83	0.29–2.35	0.725
ICS use	1.74	0.66–4.60	0.263
NLR	0.88	0.58–1.35	0.564
METS-IR, per unit	0.96	0.90–1.03	0.254

Outcome variable: eosinophilic asthma, defined as a peripheral blood eosinophil count ≥ 300 cells/ μL . Independent variables entered into the multivariable logistic regression model were age, sex, inhaled corticosteroid (ICS) use, neutrophil-to-lymphocyte ratio (NLR), and metabolic score for insulin resistance (METS-IR). Odds ratios (ORs) are adjusted for all variables included in the model.

Table 7. Assessment of multicollinearity.

Predictor	Tolerance	VIF
Age	0.867	1.15
Female sex	0.962	1.04
ICS use	0.929	1.08
NLR	0.938	1.07
METS-IR	0.924	1.08

ICS: inhaled corticosteroid; METS-IR: metabolic score for insulin resistance; NLR: neutrophil-to-lymphocyte ratio; VIF: variance inflation factor.

Discussion

In this retrospective cross-sectional study, we investigated the relationship between metabolic dysfunction and eosinophilic asthma using multiple insulin resistance-related indices. Three principal findings emerged. First, patients with asthma exhibited significantly greater metabolic dysfunction and systemic inflammatory burden than healthy controls. Second, eosinophilic and non-eosinophilic asthma phenotypes differed significantly in BMI and METS-IR values, with patients with non-eosinophilic asthma demonstrating a greater obesity-related metabolic burden. Third, although these differences remained evident in univariate analyses, the associations were attenuated after adjustment for potential confounding factors in the multivariable logistic regression model.

The association between obesity and asthma has been extensively documented [6, 7]. However, contemporary evidence indicates that obesity-related asthma should not be viewed merely as asthma occurring in individuals with excess body weight. Rather, it represents a biologically distinct phenotype characterized by metabolic abnormalities, systemic inflammation, altered immune responses, and reduced corticosteroid responsiveness. Obesity-related airway disease is frequently associated with neutrophilic or paucigranulocytic inflammation and lower expression of classical type-2 inflammatory biomarkers [5]. Our findings are consistent with this concept, as patients with non-eosinophilic asthma exhibited higher BMI and METS-IR values in the univariate analyses, although these associations were attenuated after multivariable adjustment.

Several biological mechanisms may explain these observations. Adipose tissue functions as an active endocrine organ that produces adipokines, pro-inflammatory cytokines, and mediators involved in insulin resistance. Chronic metabolic inflammation may alter airway immune responses through increased production of interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), leptin, oxidative stress, and dysregulated macrophage activation, together with reduced adiponectin levels [5–7]. Rather than promoting classical type-2 eosinophilic inflammation, these metabolic alterations predominantly activate innate immune pathways and are thought to favor neutrophilic or paucigranulocytic airway inflammation. In addition, obesity-related metabolic dysfunction may impair airway function through mechanisms independent of eosinophilic inflammation, including reduced lung compliance, increased airway closure, altered respiratory mechanics, and airway remodeling associated with insulin resistance and mitochondrial dysfunction. Consequently, obesity-related metabolic abnormalities may be more closely linked to non-eosinophilic asthma, a phenotype frequently characterized by corticosteroid resistance, persistent symptoms, and poorer clinical outcomes. These findings suggest that metabolic dysfunction may contribute to asthma phenotype differentiation rather than uniformly increasing eosinophilic inflammation, although the underlying mechanisms could not be directly evaluated in the present study.

Although METS-IR was not independently associated with eosinophilic asthma after adjustment, it consistently showed lower values among eosinophilic patients in the univariate analyses. Unlike HOMA-IR, TyG, and CHG, METS-IR integrates anthropometric measures of adiposity together with glucose and lipid metabolism, thereby providing a more comprehensive representation of obesity-related metabolic burden [9]. Similarly, BMI directly reflects excess adiposity, whereas HOMA-IR, TyG, and CHG primarily reflect insulin resistance through glucose- and lipid-based parameters. Because obesity-related asthma is driven not only by insulin resistance but also by excess adiposity, systemic inflammation, and metabolic

dysregulation, indices incorporating anthropometric components may better capture the biological processes underlying asthma phenotypic heterogeneity. Although the independent association was attenuated after adjustment, the consistent differences observed in univariate analyses suggest that composite metabolic indices such as METS-IR may provide complementary information for characterizing the complex interaction between metabolism and asthma phenotypes.

The clinical implications of these findings are noteworthy. Patients with high metabolic burden may represent a subgroup with obesity-related non-eosinophilic asthma, a phenotype often characterized by poorer symptom control, lower responsiveness to ICSs, and fewer therapeutic options than eosinophilic disease. Identification of metabolic dysfunction in routine clinical practice may therefore facilitate more personalized management strategies emphasizing weight reduction, physical activity, dietary modification, and optimization of metabolic health in addition to conventional pharmacological therapy. These findings may help clinicians identify patients who require closer metabolic assessment and integrated management of obesity-related comorbidities alongside standard asthma care.

Our study has several limitations. The retrospective cross-sectional design precludes causal inference, and reverse causality cannot be excluded. Eosinophilic phenotype was defined using peripheral blood eosinophil counts rather than sputum eosinophils or fractional exhaled nitric oxide. Historical eosinophil counts were not consistently available; therefore, persistence of eosinophilia over time could not be confirmed. Given the known temporal variability of blood eosinophil counts, some degree of phenotype misclassification is possible. In addition, information regarding asthma severity, pulmonary function parameters, physical activity, dietary habits, and cumulative corticosteroid exposure was not available. Nevertheless, this study is among the first to simultaneously evaluate multiple metabolic indices in relation to eosinophilic asthma phenotype while including a healthy control group for comparison.

Patients with asthma exhibited greater metabolic dysfunction than healthy controls. Although eosinophilic asthma was associated with lower BMI and METS-IR values in univariate analyses, these associations were not confirmed after adjustment for potential confounders. Larger prospective studies are warranted to further investigate the relationship between metabolic dysfunction and asthma phenotypes.

Abbreviations

BMI: body mass index

CHG: cholesterol-glucose

HDL-C: high-density lipoprotein cholesterol

HOMA-IR: homeostatic model assessment for insulin resistance

ICSs: inhaled corticosteroids

METS-IR: metabolic score for insulin resistance

NLR: neutrophil-to-lymphocyte ratio

TyG: triglyceride-glucose

VIFs: variance inflation factors

Declarations

Author contributions

EFÖP: Conceptualization, Methodology, Formal analysis, Writing—original draft, Writing—review & editing, Project administration. Üİİ: Investigation, Data curation, Resources, Writing—review & editing. FG: Investigation, Resources, Validation, Writing—review & editing. YS: Investigation, Validation, Writing—review & editing. HB: Methodology, Validation, Writing—review & editing. UB: Conceptualization, Methodology, Supervision, Validation, Writing—review & editing. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical approval

This study was approved by the Non-Interventional Clinical Research Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (Decision No. 29, dated June 16, 2026). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent to participate

Informed consent to publication was obtained from relevant participants.

Consent to publication

Not applicable.

Availability of data and materials

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

Funding

Not applicable.

Copyright

© The Author(s) 2026.

Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

References

1. Jayasooriya SM, Devereux G, Soriano JB, Singh N, Masekela R, Mortimer K, et al. Asthma: epidemiology, risk factors, and opportunities for prevention and treatment. *Lancet Respir Med*. 2025;13:725–38. [DOI] [PubMed]
2. Venkatesan P. 2023 GINA report for asthma. *Lancet Respir Med*. 2023;11:589. [DOI] [PubMed]
3. Gill BA, Ijaz A, Fatima N, Ahmed A, Noor A, Sharif S, et al. Efficacy and safety of Depemokimab in asthma with eosinophilic phenotype: a systematic review and meta-analysis of randomized controlled trials. *BMC Immunol*. 2025;27:2. [DOI] [PubMed] [PMC]
4. Lommatzsch M, Buhl R, Bergmann KC, Brusselle GG, Canonica GW, Jackson DJ, et al. Eosinophils in asthma phenotypes: perpetrators or guilty by association? *Lancet Respir Med*. 2025;13:943–50. [DOI] [PubMed]
5. Riemann S, Matthys I, Maes T, Lapauw B, Brusselle G. Obesity and asthma: obesity causes and aggravates asthma across the entire type-2 inflammation spectrum. *Eur Respir J*. 2026;67:2502687. [DOI] [PubMed] [PMC]
6. Menegati LM, de Oliveira EE, Oliveira BC, Macedo GC, de Castro E Silva FM. Asthma, obesity, and microbiota: A complex immunological interaction. *Immunol Lett*. 2023;255:10–20. [DOI] [PubMed]
7. Althoff MD, Gaietto K, Holguin F, Forno E. Obesity-related Asthma: A Pathobiology-based Overview of Existing and Emerging Treatment Approaches. *Am J Respir Crit Care Med*. 2024;210:1186–200. [DOI] [PubMed] [PMC]

8. Chen Y, Yang J, Han K, Wang Y, Zhuang C, Zhu L, et al. An Elevated METS-IR Index Is Associated With Higher Asthma Morbidity and Earlier Age of First Asthma in US Adults: Results Based on a Cross-Sectional Study. *Front Endocrinol (Lausanne)*. 2022;13:920322. [DOI] [PubMed] [PMC]
9. Duan M, Zhao X, Li S, Miao G, Bai L, Zhang Q, Yang W, Zhao X, et al. Metabolic score for insulin resistance (METS-IR) predicts all-cause and cardiovascular mortality in the general population: evidence from NHANES 2001-2018. *Cardiovasc Diabetol*. 2024;23:243. [DOI] [PubMed] [PMC]
10. Thomas DM, Bredlau C, Bosy-Westphal A, Mueller M, Shen W, Gallagher D, et al. Relationships between body roundness with body fat and visceral adipose tissue emerging from a new geometrical model. *Obesity (Silver Spring)*. 2013;21:2264–71. [DOI] [PubMed] [PMC]
11. Alizargar J, Bai CH, Hsieh NC, Wu SV. Use of the triglyceride-glucose index (TyG) in cardiovascular disease patients. *Cardiovasc Diabetol*. 2020;19:8. [DOI] [PubMed] [PMC]
12. Çatak M, Konuk ŞG, Hepsen S. The cholesterol-HDL-glucose (CHG) index and traditional adiposity markers in predicting diabetic retinopathy and nephropathy. *J Diabetes Investig*. 2025;16:1487–94. [DOI] [PubMed] [PMC]
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28:412–9. [DOI] [PubMed]
14. Yoon J, Jung D, Lee Y, Park B. The Metabolic Score for Insulin Resistance (METS-IR) as a Predictor of Incident Ischemic Heart Disease: A Longitudinal Study among Korean without Diabetes. *J Pers Med*. 2021;11:742. [DOI] [PubMed] [PMC]