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Association between eosinophil number and overweight status: a nonlinear, bidirectional study

Xinghai Yue[1†], Chenchen Wang[1†] and Xixu Zhang[2*]

Abstract

Background The relationship between eosinophil number and overweight status (or obesity) remains a subject of debate. While animal studies suggest a negative correlation between the two, most clinical studies indicate a positive correlation. Therefore, we hypothesize that a nonlinear relationship may exist between eosinophil number and overweight status. This study aims to investigate the association between eosinophil number and overweight status (as well as related indicators) using data from the National Health and Nutrition Examination Survey (NHANES).

Methods We utilized data from NHANES 1999–2018, where eosinophil number was obtained from laboratory tests. Overweight status was defined as a body mass index (BMI) ≥ 25. We then applied weighted logistic regression/linear regression, subgroup analysis, and restricted cubic splines (RCS) analysis to investigate the association between eosinophil number and overweight status (as well as related indicators).

Results A total of 77,217 individuals were included in this study, with 38,106 individuals in the non-overweight group (BMI < 25) and 39,111 individuals in the overweight group (overweight and obesity, BMI ≥ 25). The logistic regression analysis revealed a significant association between eosinophil number and overweight status (OR: 2.38, 95% CI: 1.81–3.12, $P < 0.001$). Additionally, eosinophil number was significantly positively correlated with obesity/BMI/triglycerides and negatively correlated with High-Density Lipoprotein (HDL). Finally, the nonlinear regression results indicated an inverted U-shaped relationship between eosinophil number and overweight status/obesity/BMI.

Conclusion Our study demonstrates an inverted U-shaped relationship between eosinophil number and overweight status/obesity/BMI. Eosinophil number is also significantly associated with HDL and triglycerides. These findings suggest that eosinophils may play a role in overweight (or obesity) and provide valuable insights for exploring the underlying immune mechanisms of overweight status.

Keywords Eosinophil, Overweight, Body mass index, Obesity, NHANES

[†]Xinghai Yue and Chenchen Wang these authors share the first authorship.

*Correspondence:
Xixu Zhang
zhangxixu1987@163.com
[1]The Second Clinical College, Liaoning University of Traditional Chinese Medicine, Shenyang, Liaoning, China
[2]Department of Endocrinology, The Second Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang, Liaoning, China

Introduction

With the continuous rise in global obesity rates, overweight and obesity have become significant public health concerns [1, 2]. Studies have shown that overweight and obesity not only increase the risk of chronic diseases such as cardiovascular diseases [3–5] and diabetes [6–8], but are also closely associated with various other conditions [9–11], including allergic diseases [12–14].

Currently, the incidence of allergic diseases is also on the rise [15], and growing evidence suggests a complex interaction between obesity and allergic diseases [16–18]. Genetic studies have revealed shared genetic components between obesity and allergic diseases [19], and another Mendelian randomization study has demonstrated a complex causal relationship between obesity and conditions such as asthma and atopic dermatitis [20]. Moreover, individuals with obesity are often in a state of chronic inflammation, characterized by elevated levels of various inflammatory mediators, including tumor necrosis factor-alpha (TNF-α) and multiple interleukins (ILs) [21], which may further increase the risk of developing allergic diseases. Dysbiosis of gut microbiota has also been identified as a key link between obesity and immune dysregulation [17, 18], further contributing to the development of allergic diseases.

Eosinophils are important immune cells involved in allergic diseases [22, 23], participating in various stages of allergic and inflammatory responses. As a clinical indicator for monitoring allergic conditions, fluctuations in eosinophil counts often reflect the degree of allergic activation. Notably, studies have shown that eosinophils not only play a role in allergic inflammation but also serve important functions in metabolic regulation. They contribute to metabolic homeostasis by maintaining adipose alternatively activated macrophages (AAMs) [24] and directly regulating lipid metabolism [25]. In the context of obesity, dysregulation of eosinophil function may represent a key mechanism linking metabolic disorders and allergic diseases. Given the close association among obesity, allergic diseases, and eosinophils, the relationship between eosinophils and overweight status also warrants further investigation.

Previous studies have shown conflicting results regarding the association between eosinophils and obesity. Several animal studies have suggested a negative correlation between eosinophil levels and obesity [26–28]. For instance, a study by Davina Wu et al. in 2011 [24] found that high-fat diet mice lacking eosinophils were more prone to obesity, impaired glucose tolerance, and insulin resistance. In 2020, Daniel Brigger et al. [29] reported that transplantation of eosinophils from young mice into aged mice alleviated systemic low-grade inflammation in the latter. Additionally, another study [25] found that mice with inhibition of Krüppel-like factor 3 (KLF3) had higher eosinophil levels in adipose tissue and lower body weight. These findings highlight the important regulatory role of eosinophils in adipose tissue and suggest their potential in reducing the risk of obesity. However, most clinical studies have reported a positive correlation between eosinophils and obesity [30–32]. A cross-sectional study from China involving 62,441 healthy participants [33] also demonstrated that eosinophil levels were significantly associated with higher levels of low-density lipoprotein and triglycerides, as well as lower levels of high-density lipoprotein, and this association was influenced by BMI.

The reasons for the discrepancy between animal experiments and clinical findings remain unclear. On one hand, the relatively short duration of animal studies and the limited generalizability of animal models may fail to fully capture the complexity of human metabolic and immune environments. On the other hand, the inconsistency may also be attributed to the context-specific roles of eosinophils in different tissue environments, as well as potential confounding factors in population-based studies.

One possible explanation is that a nonlinear relationship between eosinophil count and overweight status may exist, wherein eosinophils exert different biological effects at different levels, possibly due to threshold effects. Despite growing interest in this topic, most clinical studies have only explored linear associations and may have overlooked more complex, nonlinear patterns. In addition, previous studies often suffered from limited sample sizes, potentially missing subtle associations.

To address these limitations, we utilized data from NHANES. NHANES is a nationwide survey conducted by the Centers for Disease Control and Prevention (CDC) in the United States. By conducting physical examinations, interviews, and laboratory tests on a representative sample of the U.S. population, NHANES collects data on health, nutrition, chronic diseases, and environmental factors. The survey employs a complex sampling method to ensure that the selected individuals are sufficiently representative, making it highly valuable for clinical research.

Therefore, the aim of this study was to investigate the association between eosinophil count and overweight status, as well as related metabolic indicators, using a large-scale, population-based dataset. Specifically, we aimed to assess potential nonlinear relationships and explore subgroup differences, thereby providing new insights into the immunometabolic interactions involved in obesity.

Methods

Data Source

The population data for this study were sourced from NHANES 1999–2018. We included individuals with

complete data on blood eosinophil counts and BMI. Figure 1 presents the data selection flowchart for this study. Since weighted data were used in the analysis, no imputation was performed for missing data.

The unit for eosinophil number was 1000 cells/uL. Following the World Health Organization's standards [34], overweight status was defined as individuals with a BMI ≥ 25, and obesity was defined as individuals with a BMI ≥ 30. Additionally, we extracted other indicators related to overweight status, including Low-Density Lipoprotein (LDL), total cholesterol (TCHOL), plasma glucose (GLU), High-Density Lipoprotein (HDL), and triglycerides.

Covariates

This study also selected the following covariates: age, sex [35], race [36.37], educational level [38], marital status [39], poverty income ratio (PIR) index [40], creatinine levels [41], serum cotinine levels [42], alcohol consumption status [43], self-reported hypertension [44], self-reported coronary heart disease [45], and self-reported diabetes [46]. Among these, the classification of race was based on the default categories provided by NHANES and does not carry any additional or specific implications, the PIR index was used as a proxy for economic status, and serum cotinine level was used as a proxy for smoking status [47, 48]. For marital status, we classified "Married, Living with partner" as Non-single, and "Widowed, Divorced, Separated, Never married" as Single. For alcohol consumption, individuals who had not consumed alcohol in the past year were categorized as non-drinkers, while others were classified as drinkers. The detailed NHANES codes used in this study can be found in Supplementary Table S1.

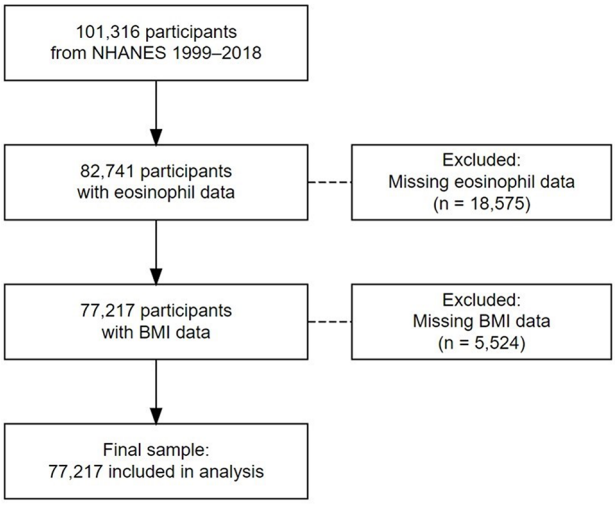

Fig. 1 Flowchart of Participant Selection for the NHANES 1999–2018

Statistical Analysis

All analyses in this study were conducted under weighted conditions. The weighted variable used in this study was WTMEC2YR, which was adjusted according to the selected survey cycle by dividing by 10. Statistical tests are based on weighted data using the survey design. Continuous variables were compared using weighted t-tests (svyttest), and categorical variables using Rao–Scott chi-square tests. Weighted multivariable logistic regression was then employed to explore the association between eosinophil number and overweight status. Subgroup analysis was conducted to examine how this association varied across different groups. Subsequently, we analyzed the association between eosinophil number and overweight-related indicators, including obesity, BMI, GLU, LDL, TCHOL, HDL, and triglycerides. Finally, RCS with 5 knots were used to explore the nonlinear relationship between eosinophil number and overweight status/obesity/BMI. In the RCS analysis, the overall association between the variable and the outcome (including both linear and nonlinear components) was evaluated using the *P overall*, while the presence of a significant nonlinear relationship was assessed using the *P for non-linear*.

The R packages used in this paper include survey (4.4.2), gtsummary (2.0.2), forestploter (1.1.2), rms (6.8-1), ggplot2 (3.5.1), tableone (0.13.2). The statistical analyses in this study were conducted using R version 4.4.1.

Results

Baseline characteristics

A total of 77,217 individuals were included in this study, with detailed information provided in Table 1. This study employed weighted analyses; therefore, all P-values presented in Table 1 are based on weighted analyses. The overall mean age was 34 years, with a mean BMI of 26 kg/m^2. The average eosinophil count was 0.22×10^3 cells/uL. The weighted characteristics of the participants can be found in the supplementary file (Table S2).

Among them, 38,106 were classified as non-overweight (BMI < 25) and 39,111 as overweight status (BMI ≥ 25). Compared to the overweight group, the non-overweight individuals were younger (mean age: 23 vs. 45 years), had a lower average BMI (20 vs. 32), and a comparable eosinophil count (0.22 vs. 0.21). Notably, 73% of the non-overweight group were under 30 years old, while 42% of the overweight group were aged 30–59 years.

Logistic regression results

The logistic regression results (Fig. 2) showed a significant positive association between eosinophil number and overweight status (OR: 2.38, 95% CI: 1.81–3.12, $P < 0.001$). Furthermore, the results indicated significant associations between overweight status and factors such as gender, race, education level, marital status, alcohol

Table 1 Basic characteristics of participants by overweight status

Characteristic	Overall *N* = 77,217	Non-overweight *N* = 38,106	Overweight Status *N* = 39,111	*P*-value*
Age (mean (SD))	34 (24)	23 (22)	45 (20)	< 0.001
Age group (%)				< 0.001
< 30	38,409 (50%)	27,668 (73%)	10,741 (27%)	
30–59	22,661 (29%)	6,168 (16%)	16,493 (42%)	
≥ 60	16,147 (21%)	4,270 (11%)	11,877 (30%)	
Sex (%)				< 0.001
Female	39,067 (51%)	19,181 (50%)	19,886 (51%)	
Male	38,150 (49%)	18,925 (50%)	19,225 (49%)	
EOS number (1000 cells/uL) (mean (SD))	0.22 (0.19)	0.22 (0.21)	0.21 (0.17)	< 0.001
EOS percentage (mean (SD))	3.04 (2.44)	3.22 (2.75)	2.85 (2.08)	0.958
Race (%)				< 0.001
Mexican American	17,037 (22%)	8,419 (22%)	8,618 (22%)	
Non-Hispanic Black	17,840 (23%)	8,940 (23%)	8,900 (23%)	
Non-Hispanic White	29,081 (38%)	13,499 (35%)	15,582 (40%)	
Other Hispanic	6,318 (8.2%)	2,914 (7.6%)	3,404 (8.7%)	
Other Race	6,941 (9.0%)	4,334 (11%)	2,607 (6.7%)	
Educational level (%)				< 0.001
Under high school	12,512 (27%)	3,338 (24%)	9,174 (28%)	
High school or equivalent	10,873 (23%)	3,077 (22%)	7,796 (24%)	
Above high school	23,606 (50%)	7,543 (54%)	16,063 (49%)	
Marital status (%)				< 0.001
Non-single	28,717 (54%)	8,086 (45%)	20,631 (59%)	
Single	23,994 (46%)	9,708 (55%)	14,286 (41%)	
PIR (mean (SD))	2.32 (1.60)	2.20 (1.60)	2.43 (1.60)	< 0.001
PIR group (%)				< 0.001
< 1	18,279 (26%)	10,229 (29%)	8,050 (22%)	
≥ 1	52,808 (74%)	25,027 (71%)	27,781 (78%)	
BMI (mean (SD))	26 (7)	20 (3)	32 (6)	< 0.001
BMI group (%)				< 0.001
Under weight	13,494 (17%)	13,494 (35%)	0 (0%)	
Normal weight	24,612 (32%)	24,612 (65%)	0 (0%)	
Overweight	19,549 (25%)	0 (0%)	19,549 (50%)	
Obesity	19,562 (25%)	0 (0%)	19,562 (50%)	
Log2 Cotinine (ng/mL) (mean (SD))	-2.1 (4.9)	-2.3 (4.7)	-1.9 (5.1)	0.157
Log2 Cotinine group (%)				< 0.001
< 0.05	55,275 (75%)	26,901 (76%)	28,374 (74%)	
0.05-3	4,847 (6.6%)	2,870 (8.2%)	1,977 (5.1%)	
≥ 3	13,631 (18%)	5,425 (15%)	8,206 (21%)	
Creatinine (umol/L) (mean (SD))	75 (35)	71 (33)	77 (36)	< 0.001
Plasma glucose (mmol/L) (mean (SD))	5.81 (1.84)	5.38 (1.33)	6.08 (2.06)	< 0.001
LDL (mmol/L) (mean (SD))	2.81 (0.91)	2.59 (0.85)	2.97 (0.92)	< 0.001
TCHOL (mmol/L) (mean (SD))	4.75 (1.07)	4.46 (0.97)	4.99 (1.10)	< 0.001
HDL (mmol/L) (mean (SD))	1.37 (0.39)	1.47 (0.38)	1.28 (0.37)	< 0.001
Triglycerides (mmol/L) (mean (SD))	1.54 (1.27)	1.12 (0.81)	1.80 (1.43)	< 0.001
Alcohol drinker (%)				< 0.001
Yes	29,953 (78%)	9,346 (82%)	20,607 (76%)	

Table 1 (continued)

Characteristic	Overall *N* = 77,217	Non-overweight *N* = 38,106	Overweight Status *N* = 39,111	*P*-value*
No	8,489 (22%)	2,069 (18%)	6,420 (24%)	
Diabetes (%)				< 0.001
Yes	5,590 (7.2%)	836 (2.2%)	4,754 (12%)	
No	71,578 (93%)	37,246 (98%)	34,332 (88%)	
Hypertension (%)				< 0.001
Yes	16,271 (30%)	3,024 (17%)	13,247 (37%)	
No	37,876 (70%)	15,239 (83%)	22,637 (63%)	
Coronary heart disease (%)				< 0.001
Yes	1,888 (4.0%)	421 (3.0%)	1,467 (4.5%)	
No	44,961 (96%)	13,515 (97%)	31,446 (96%)	
Asthma, n (%)				0.005
Yes	11,261 (15%)	5,321 (14%)	5,940 (15%)	
No	65,887 (85%)	32,746 (86%)	33,141 (85%)	

*All p-values are based on weighted analyses. Continuous variables were compared using weighted t-tests (svyttest), and categorical variables using Rao–Scott chi-square tests. PIR: Poverty Income Ratio, BMI: Body Mass Index, LDL: Low-Density Lipoprotein, TCHOL: Total Cholesterol, HDL: High-Density Lipoprotein

consumption, diabetes, and hypertension. Although age and serum cotinine levels were also significantly associated with overweight status, the effect sizes for these variables were minimal.

We also conducted an association analysis between eosinophil percentage and overweight status, but the results showed no significant association. (OR: 1.006,95%CI:0.989–1.023, $P = 0.514$). Therefore, eosinophil percentage was not included in subsequent analyses. Detailed results can be found in Supplementary Table S3.

Analysis of related indicators

To minimize the potential errors caused by collinearity among related variables, we also conducted separate analyses of eosinophil number and several related indicators, including obesity, blood glucose, LDL, total cholesterol (TCHOL), HDL, and triglycerides, as shown in Table 2. The results indicated significant associations between eosinophil number and multiple indicators, including obesity (OR: 2.33, 95% CI: 1.96–2.77, $P < 0.001$), BMI (β: 3.11, 95% CI: 2.55–3.67, $P < 0.001$), HDL (β: -0.22, 95% CI: -0.26 to -0.19, $P < 0.001$), and triglycerides (β: 0.48, 95% CI: 0.37 to 0.59, $P < 0.001$).

Additionally, we conducted a reverse analysis to investigate the effect of BMI-related indicators on eosinophil number. Although some results were significant, the effect sizes were very small. (e.g. Overweight Status–EOS number, β = 0.018, 95% CI: 0.013 to 0.023, $P < 0.001$). Detailed results can be found in Supplementary Table S3.

Subgroup analysis

The results of the subgroup analysis are shown in Fig. 3. (In addition to overweight status, subgroup analyses were extended to include obesity and BMI. The results can be found in the supplementary file Figures S1–S2). The findings indicate that the association between eosinophil number and overweight status was significant in most subgroups. It is noteworthy that this association was particularly evident in the groups aged 30–59 years, female, Mexican American, with a high school education or above, non-single, log2 cotinine levels below 0.05, and non-drinkers, all of which had OR values greater than 3. This indicates that for each increase of 1 in eosinophil number, the risk of overweight status in these groups increased by more than threefold.

Furthermore, significant interaction effects were observed in the subgroup analysis of eosinophils and overweight status for several factors, including sex, race, PIR index, educational level, and marital status. This indicates that the association between eosinophils and overweight status varies significantly across these subgroups. A possible explanation, supported by previous literature, is that certain subpopulations are more susceptible to obesity, which is characterized by chronic low-grade inflammation that may amplify the role of eosinophils. Our subgroup analysis of eosinophils and BMI revealed similar findings (Supplementary File, Figure S2), with the effect of eosinophils on BMI being more pronounced in obese individuals (β: 1.77 95%CI: 0.99–2.55, $P < 0.001$).

Specifically, in terms of sex, studies have shown that women are more likely than men to develop obesity [35]. As for race, it is well established that the prevalence of obesity varies across racial groups [37], although the underlying mechanisms remain unclear. Marital status is another factor, with several analyses suggesting that married individuals are more likely to be obese [39].

However, contrary to our expectations, subgroup analyses based on socioeconomic status (PIR index) [40] and educational level [38] showed that the effect of eosinophils on overweight status was more significant in populations with higher PIR scores and higher educational attainment, which warrants further investigation.

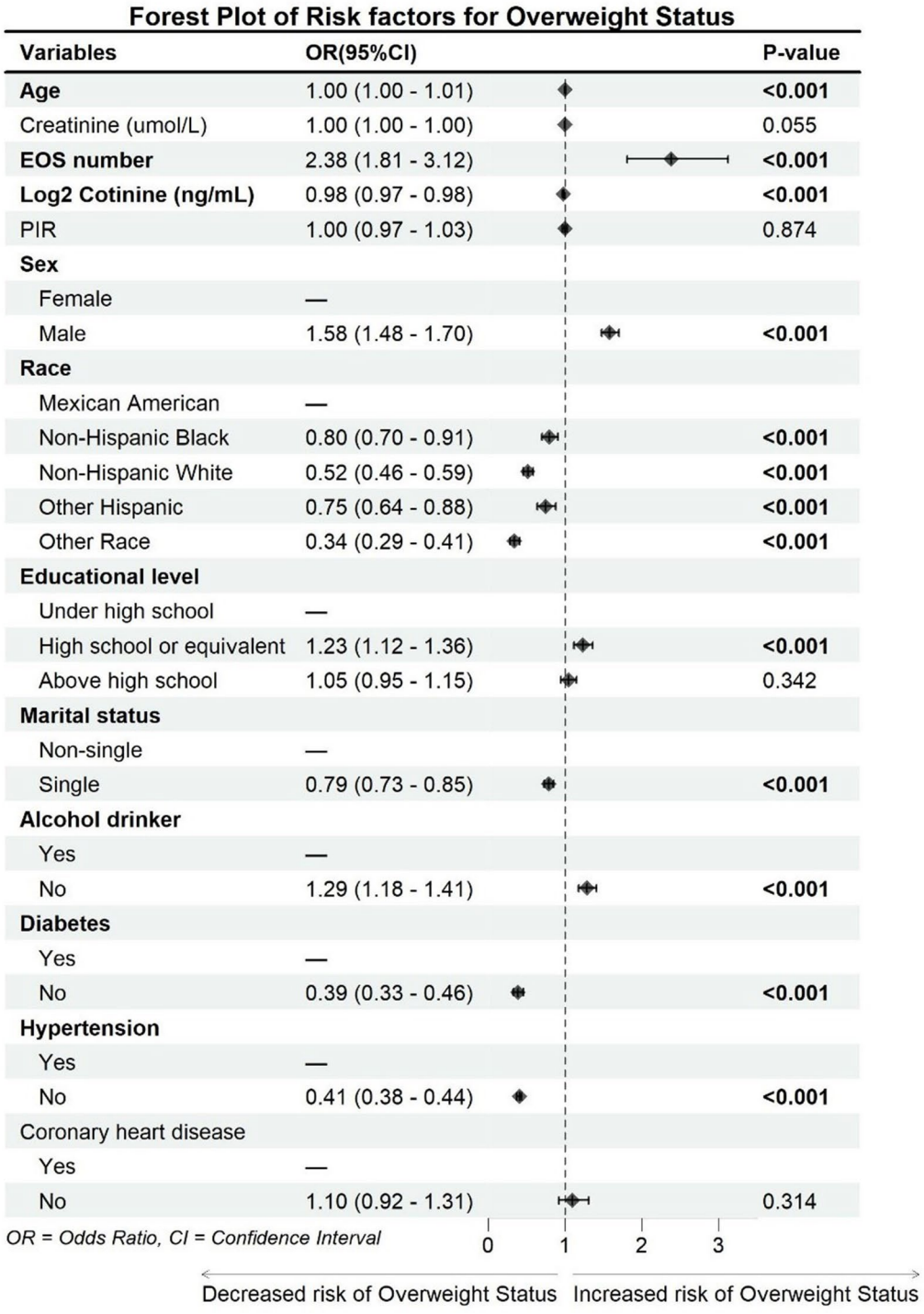

Fig. 2 Forest plot of risk factors for overweight status

RCS analysis

We conducted restricted cubic spline (RCS) analyses of eosinophil number and overweight status/obesity/BMI (Figs. 3, 4, 5 and 6). The results showed that in all three RCS analyses, both the P overall and P for non-linear values were less than 0.001, indicating that eosinophils were associated with overweight status, obesity, and BMI through both linear and nonlinear relationships. The three results were similar, all showing an inverted U-shaped curve. In our study, 72.43% of the population had eosinophil numbers between 0 and 0.2 × 1000 cells/uL (inclusive of 0.2), 22.75% had counts between 0.3 and 0.5, 4.18% had counts between 0.6 and 1, and 0.68% had counts greater than 1. The average eosinophil number for

Table 2 Analysis results of eosinophils in relation to obesity and its associated indicators

	Variable	Outcome	OR	95% CI	*P*-value
Model 1	EOS number	Obesity	2.33	1.96, 2.77	**< 0.001**
	Variable	**Outcome**	**Beta**	**95% CI**	**P-value**
Model 2	EOS number	BMI	3.11	2.55, 3.67	**< 0.001**
Model 3	EOS number	GLU	0.10	-0.04, 0.25	0.173
Model 4	EOS number	LDL	0.00	-0.12, 0.12	0.985
Model 5	EOS number	TCHOL	0.00	-0.09, 0.09	0.968
Model 6	EOS number	HDL	-0.22	-0.26, -0.19	**< 0.001**
Model 7	EOS number	Triglycerides	0.48	0.37, 0.59	**< 0.001**

All models were adjusted for the following covariates: sex, age, log2 cotinine, creatinine PIR, race, education level, marital status, alcohol consumption, diabetes, hypertension, and coronary heart disease. BMI: Body Mass Index, GLU: Plasma glucose, LDL: Low-Density Lipoprotein, TCHOL: Total Cholesterol, HDL: High-Density Lipoprotein.

all individuals was 0.22. In summary, this suggests that changes in eosinophil number between 0 and 1×1000 cells/uL should be the focus of the nonlinear association.

Additionally, we performed a reverse RCS analysis between BMI and eosinophil number, which revealed only a positive linear association with a small effect size. The results can be found in Supplementary Figure S3.

Discussion

To the best of our knowledge, this is the largest study to date investigating the association between eosinophil number and overweight status (obesity/BMI). The large sample size allowed us to observe more subtle associations between eosinophil number and overweight status (obesity/BMI). Our results indicate a significant positive association between eosinophil number and overweight status (OR: 2.38, 95% CI: 1.81–3.12, $P < 0.001$). Subsequent RCS analysis showed an inverted U-shaped nonlinear association between eosinophil number and overweight status (BMI/obesity), which may help explain the conflicting results from previous studies regarding the relationship between eosinophil number and overweight. Additionally, the significant associations observed between eosinophils and triglycerides (β: 0.48,95%CI:0.37–0.59,$P < 0.001$), as well as HDL (β: -0.22,95%CI:-0.26 to -0.19,$P < 0.001$), are consistent with prior research findings [49, 50].

In the supplementary materials, we also analyzed the association between eosinophil percentage and overweight status. However, the results showed no significant association between the two. In the reverse analysis of overweight status (obesity/BMI) and eosinophil number, although the results were significant, the effect sizes were very small. We also used RCS to analyze the reverse association between BMI and eosinophil number, and the results indicated that BMI only had a positive linear association with eosinophil number.

Currently, an increasing number of studies suggest that overweight status (obesity/BMI) is associated with chronic low-grade inflammation [51, 52]. And research has shown that eosinophils play a key regulatory role in adipose tissue homeostasis. They help mediate adipocyte thermogenesis and contribute to a balance in inflammatory processes [28, 53]. Therefore, we hypothesize that inflammation may be a key mechanism underlying the significant association between eosinophil count and overweight status (including obesity and BMI). However, this relationship is highly complex. An important factor lies in the dual role of eosinophils: while they often serve as markers of inflammation and possess pro-inflammatory capabilities—such as releasing large amounts of IL-4, IL-5, and TNF-α during allergic reactions, which can lead to tissue damage [54] and potentially contribute to the development or exacerbation of obesity—they can also exert anti-inflammatory effects. For example, eosinophils can secrete IL-13, which promotes the differentiation of anti-inflammatory macrophages in adipose tissue and thereby reduces insulin resistance [55]. A clinical study [56] also reported that eosinophil levels were associated with a reduced risk of diabetes and insulin resistance, which may indirectly influence the risk of obesity. This complexity suggests that the functions of eosinophils may vary under different physiological or pathological conditions.

Leptin is a hormone closely associated with adipose-derived factors [57], playing a role in appetite suppression and showing a positive correlation with body mass index (BMI) [58, 59]. Studies have shown that leptin can delay eosinophil apoptosis [60] and promote eosinophil migration and activation in vivo [57]. However, despite elevated leptin levels in individuals who are overweight or obese, most of these individuals exhibit leptin resistance [57]. Excessively high leptin levels can lead to receptor saturation [61], impairing leptin's ability to suppress appetite and reduce body weight. We speculate that this may also compromise leptin's capacity to delay eosinophil apoptosis.

Moreover, it is worth noting that a recent clinical study by James D. Hernandez et al. [62] on eosinophils and leptin found that, despite elevated leptin levels in the peripheral blood of obese patients, the level of eosinophils in adipose tissue was paradoxically decreased.

It can be observed that most previous clinical studies have reported a positive association between eosinophil levels and obesity, whereas James D. Hernandez et al. found a negative association between eosinophil levels in adipose tissue and obesity. This discrepancy highlights a key reason behind the conflicting results observed in animal experiments and clinical studies on eosinophils and obesity. Previous animal studies have primarily focused on the regulatory role of eosinophils within adipose

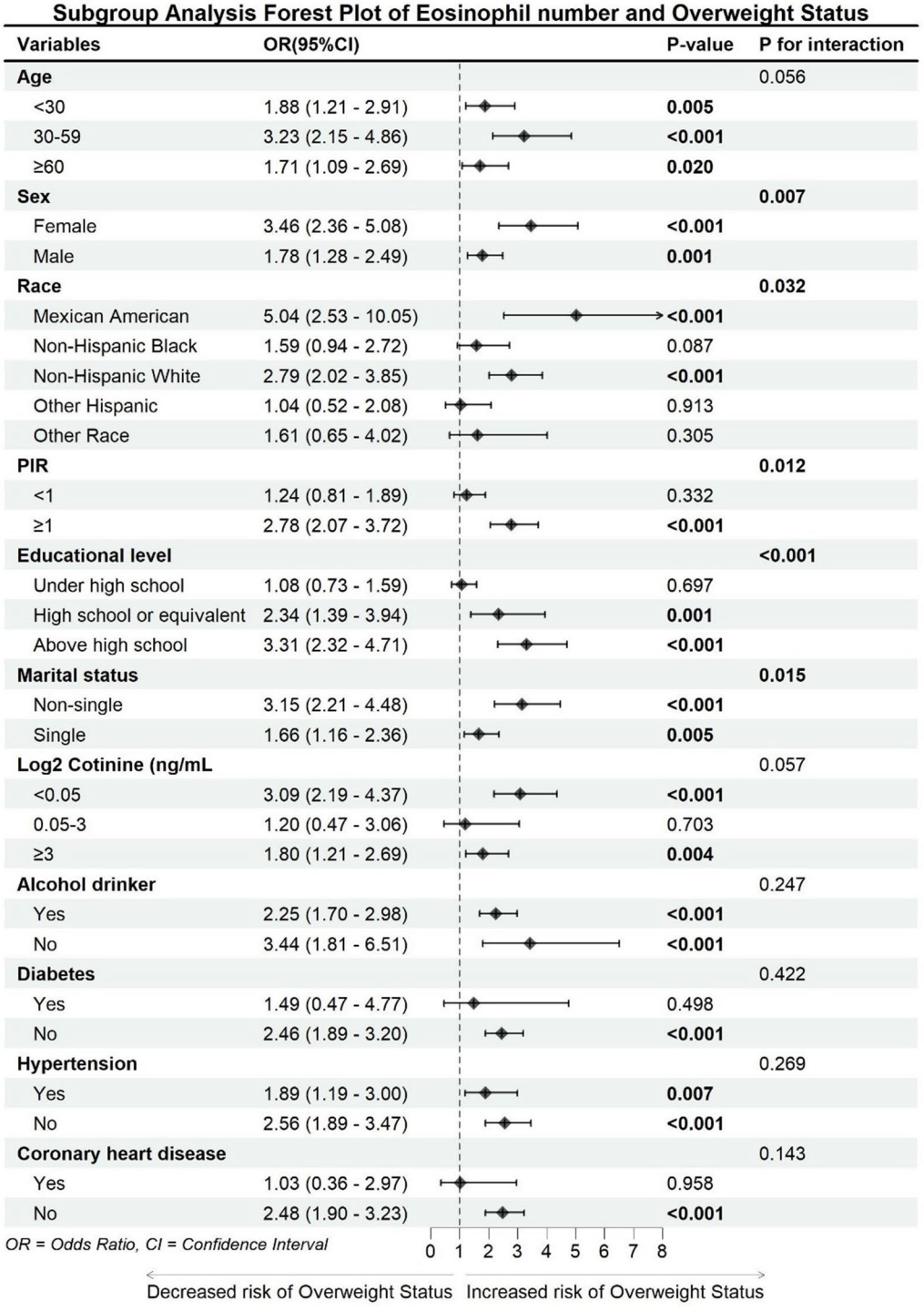

Fig. 3 Subgroup analysis forest plot of Eosinophil number and Overweight status

tissue, suggesting that eosinophils in adipose tissue contribute to the browning of white adipocytes into beige adipocytes [25, 29], thereby promoting adipose tissue catabolism. In contrast, clinical research has mostly concentrated on eosinophils in peripheral blood.

Therefore, it is reasonable to speculate that eosinophils may play distinct roles in different tissues—such as blood vs. adipose tissue, or subcutaneous vs. visceral fat—and that their distribution may vary with increasing BMI. Understanding and potentially intervening in the redistribution of eosinophils across tissues could be a key strategy for reducing obesity risk, with leptin potentially playing an important role in this process.

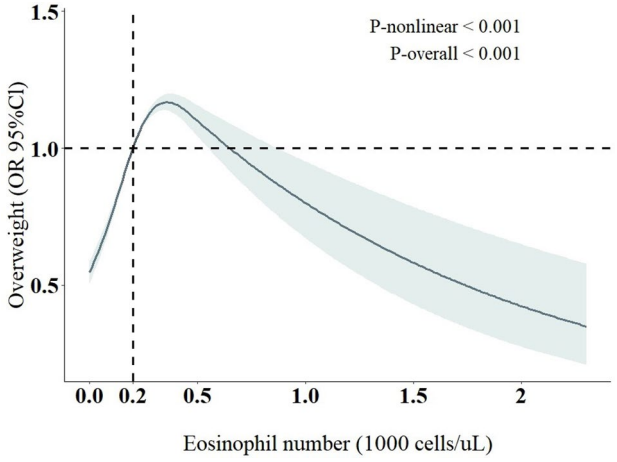

Fig. 4 Restricted Cubic Splines analysis plot of eosinophils and overweight status

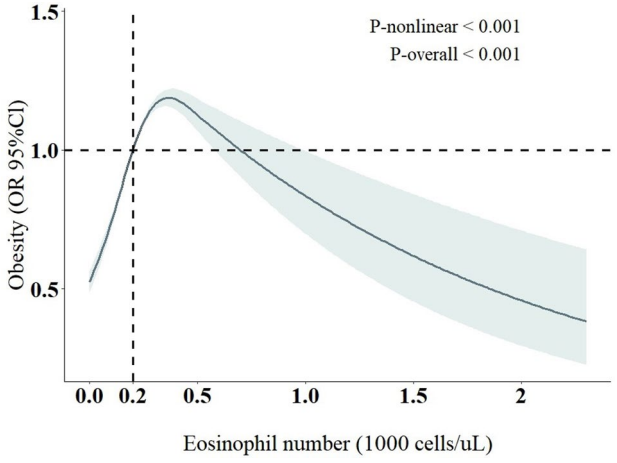

Fig. 5 Restricted Cubic Splines analysis plot of eosinophils and obesity

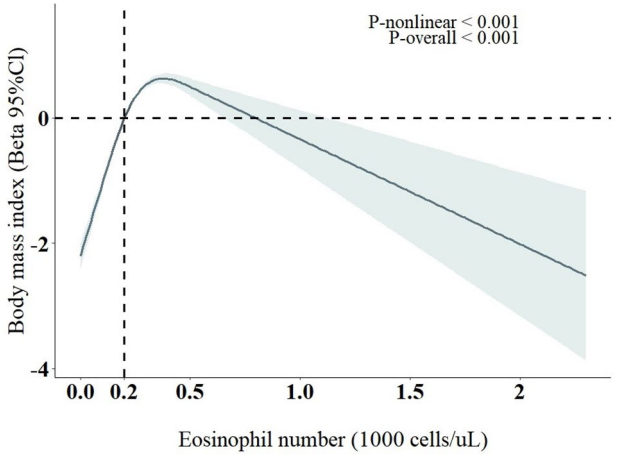

Fig. 6 Restricted Cubic Splines analysis plot of eosinophils and body mass index

Moreover, since both eosinophils and obesity are closely associated with allergic diseases, it is often assumed that allergic patients with obesity exhibit a Th2-type inflammatory profile. However, a study by Sagar P. Bapat et al. [63] demonstrated that obesity can reshape immune responses, shifting the inflammatory microenvironment toward a Th17-dominant phenotype. This finding suggests that in overweight individuals, elevated eosinophil levels may not exclusively indicate a Th2-skewed inflammation, but rather reflect a mixed inflammatory state involving both eosinophilic and Th17 pathways. The paradox lies in the fact that allergic diseases are typically accompanied by elevated eosinophil levels, and obesity is closely related to both eosinophils and allergic conditions. Given the complex interactions between immune dysregulation and metabolic states, future mechanistic studies are needed to further clarify the specific roles of Th2- and Th17-type inflammation in obesity and to determine their respective contributions to eosinophil-related outcomes.

In conclusion, our study demonstrates that there is an inverted U-shaped curve relationship between eosinophil number and overweight status (obesity/BMI), and that eosinophil number is also significantly associated with HDL and triglycerides. Although the specific mechanisms are not yet fully understood, these findings contribute to a deeper understanding of the potential role of eosinophils in obesity and related metabolic diseases. Furthermore, understanding the immunometabolic functions of eosinophils may open new avenues for early detection, risk stratification, and the development of targeted interventions for obesity and its complications.

Previous clinical studies on the relationship between eosinophils and obesity have primarily focused on specific patient populations, such as those with asthma or metabolic syndrome, while related research in the general population remains limited. Notably, a prospective cohort study from Japan [64] reported findings consistent with our results, showing a positive association between eosinophil levels and BMI at lower eosinophil concentrations, and a negative association at higher levels. However, that study was limited to a Japanese population. A major strength of the present study lies in the use of large-scale, nationally representative data from NHANES, allowing for a comprehensive evaluation of the association between eosinophil count and overweight status in the general population, as well as subgroup-specific analyses. Furthermore, we applied RCS modeling to explore potential nonlinear relationships between eosinophil count and overweight status, providing a more nuanced understanding of the association.

Nevertheless, this study has some limitations. Firstly, although we analyzed both the effect of eosinophils on overweight status and vice versa, the cross-sectional

nature of the study precludes causal inference between exposure and outcome. Future longitudinal studies are warranted to further explore this relationship. Secondly, the eosinophil number data used in our study comes from NHANES, where the values are rounded to one decimal place, which limits the precision and prevents capturing more subtle associations between eosinophil number and overweight status. Finally, the functions of eosinophils may vary across different tissues, and whether eosinophils in distinct tissues exhibit differential associations with overweight status remains an unresolved yet important question that warrants further investigation.

Conclusion

Our study demonstrates that there is an inverted U-shaped curve relationship between eosinophil number and overweight status (obesity/BMI), and that eosinophil number is also significantly associated with HDL and triglycerides. These findings suggest that eosinophils may play a role in overweight status (or obesity), providing valuable insights for further exploration of the immune mechanisms underlying overweight status, and may potentially serve as a target for future immunometabolic interventions aimed at the prevention and treatment of obesity.

Supplementary Information

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Supplementary Material 1

Author contributions

The study was designed by XH Y. The manuscript was written by XH Y, CC W and XX Z. All authors contributed to the interpretation of data and commented on the manuscript. All authors read and approved the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval

The studies involving human participants were reviewed and approved by the ethics review board of the National Center for Health Statistics. The patients/participants provided their written informed consent to participate in this study. Therefore, no additional ethical review was required for this study.

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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