

Association of lipid accumulation product, visceral adiposity index and endometriosis: A cross-sectional study from the 1999–2006 NHANES

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ABSTRACT

Introduction: Endometriosis (EMS) is a common gynaecological disorder linked to metabolic disturbances. However, evidence on the associations between lipid accumulation product (LAP) and visceral adiposity index (VAI) with the risk of EMS remains limited. This study aimed to explore the potential associations between LAP, VAI and EMS.

Methods: Data were obtained from the 1999–2006 National Health and Nutrition Examination Survey (NHANES), including a total of 2046 samples. Weighted multivariable logistic regression models and smoothed curve fitting were used to assess the associations between LAP, VAI and EMS. Additionally, subgroup analyses and interaction tests were conducted to evaluate intergroup differences in the associations between LAP, VAI and EMS.

Results: In the fully adjusted model, higher Log₂ LAP (odds ratio [OR] 1.256, 95% confidence interval [CI] 1.102–1.431, $P=0.0014$) and Log₂ VAI (OR 1.287, 95% CI 1.105–1.498, $P=0.0022$) were significantly associated with increased EMS risk. Participants in the highest quartile of Log₂ LAP (OR 1.983, $P=0.0029$) and Log₂ VAI (OR 1.690, $P=0.0486$) had a higher risk of EMS. Subgroup analysis showed stronger associations among women with diabetes (Log₂ LAP OR 3.681, $P=0.009$; Log₂ VAI OR 4.849, $P=0.041$).

Conclusion: Elevated LAP and VAI were independently associated with an increased risk of EMS. LAP and VAI may serve as potential indicators for assessing EMS-related risk, suggesting that visceral obesity and lipid metabolic disturbances might play roles in the pathophysiological process of EMS. These findings underscore the potential of LAP and VAI as non-invasive markers for EMS risk, warranting further validation in clinical settings.

Keywords: cross-sectional study, endometriosis, lipid accumulation product, NHANES, visceral adiposity index

CLINICAL IMPACT

What is New

- This study identifies higher lipid accumulation product (LAP) and visceral adiposity index (VAI) as significant independent risk factors for endometriosis (EMS).
- Elevated LAP and VAI were found to nearly double the risk of EMS, particularly in women with metabolic conditions such as diabetes.

Clinical Implications

- LAP and VAI can serve as practical, non-invasive indicators for identifying women at higher risk of EMS, facilitating early screening and intervention.
- Lifestyle modifications, including weight management and physical activity to reduce visceral fat, may help prevent or manage EMS, especially in individuals with elevated LAP and VAI.

The global prevalence among women of reproductive age is estimated at approximately 5–10%.^{1,2} Chronic pelvic pain occurs in 50–70% of EMS cases, and about 30–50% of affected women experience infertility,³ severely impacting their quality of life and reproductive health. Therefore, identifying easily accessible and reliable indicators related to EMS is crucial for early diagnosis and effective management, helping to improve women's health outcomes and reduce disease burden.

In recent years, growing evidence has suggested that metabolic disturbances—particularly those related to obesity and abnormal lipid metabolism—may play important roles in the development and progression of EMS.^{4–6} Traditional obesity measures, such as body mass index (BMI), primarily reflect overall fat content but fail to effectively distinguish fat distribution types, especially the more health-threatening visceral fat.⁷

The LAP, an index calculated based on waist circumference (WC) and fasting triglycerides (TG), was first proposed by Kahn et al. and is considered a

INTRODUCTION

EMS is a chronic, oestrogen-dependent inflammatory disease characterised by the presence of endometrial-like glands and stroma outside the uterine cavity.¹

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Accepted: 10 September 2025

Published Online First: 15 October 2025

simple yet effective marker for assessing visceral fat dysfunction and lipid accumulation.⁸ Meanwhile, the VAI combines WC, BMI, TG and high-density lipoprotein cholesterol (HDL-C) into a composite score that closely correlates with visceral fat measured by gold-standard methods,^{9,10} providing a more comprehensive reflection of visceral adiposity and showing strong associations with insulin resistance, cardiovascular disease risk and related metabolic conditions.¹¹

Previous studies have explored the associations between individual lipid components or metabolic syndrome elements and EMS. For example, a study based on National Health and Nutrition Examination Survey (NHANES) and bidirectional Mendelian randomisation found that specific lipid levels may be associated with EMS risk.¹² Another study reported a significant association between remnant cholesterol

and EMS.¹³ However, research directly examining the associations of LAP and VAI—both indicators of visceral obesity and lipid metabolic disturbances with EMS remains limited, especially in large population-based samples.

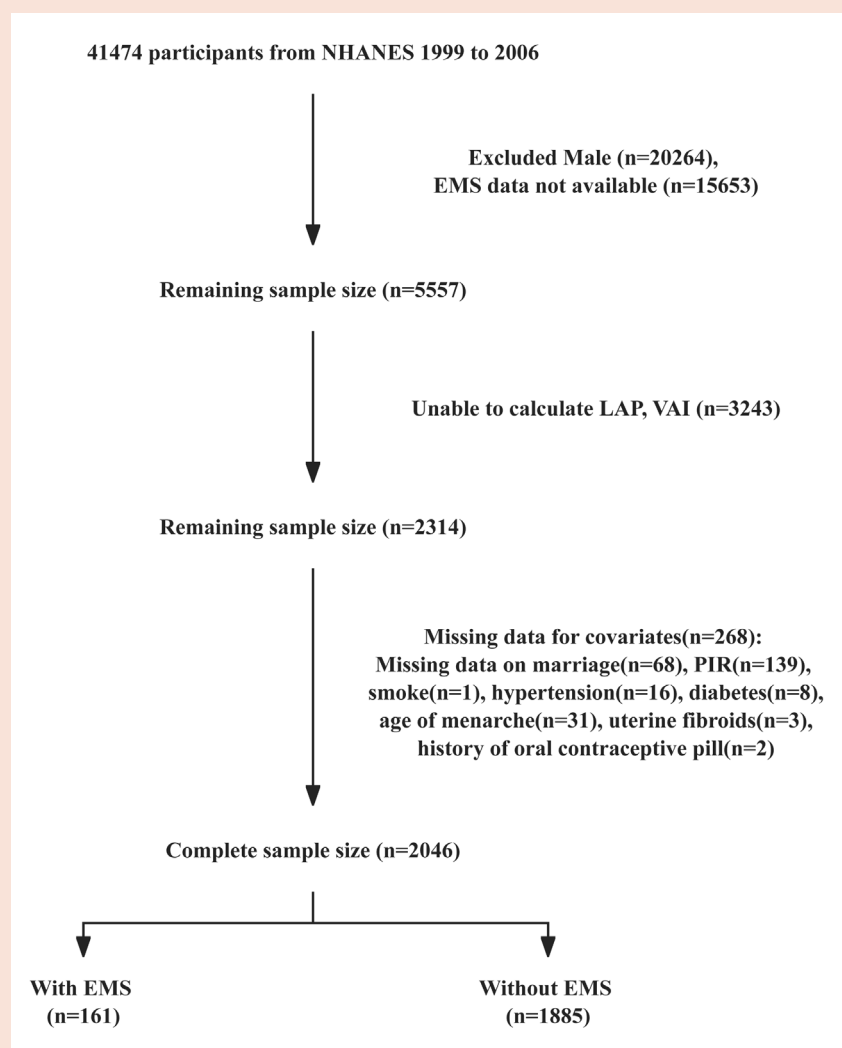
This study aims to investigate the associations between LAP, VAI and the prevalence of EMS among adult women in the US, using data from the 1999–2006 NHANES. The findings aim to provide new insights into the metabolic risk factors of EMS.

METHODS

Study dataset

This study utilised data from the NHANES 1999–2006. NHANES is a series of surveys conducted by the US National Center for Health Statistics (NCHS) using a complex, multistage probability sampling design

Fig. 1. Flowchart of participant selection from NHANES 1999–2006.



EMS: endometriosis; LAP: lipid accumulation product; NHANES: National Health and Nutrition Examination Survey; PIR: poverty income ratio; VAI: visceral adiposity index

aimed at assessing the health and nutritional status of the civilian, non-institutionalised US population (<https://www.cdc.gov/nchs/nhanes/index.htm>).

Study population

The participant selection process is detailed in Fig. 1. From an initial pool of 41,474 participants, we excluded males ($n=20,264$). Among the remaining female participants, 15,653 were excluded due to unknown EMS status, and an additional 3243 were excluded due to missing data required for LAP or VAI calculation. Participants with incomplete data on key variables were excluded to ensure analytical integrity. Finally, 268 participants were excluded because of missing covariate data. The final analytical sample included 2046 women, comprising 161 EMS cases and 1885 non-EMS controls.

Assessment of LAP and VAI

LAP and VAI were the exposure variables in this study and were calculated using the following formulas.¹⁴

$$\text{LAP} = [\text{WC}(\text{cm}) - 58] \times \text{TG}(\text{mmol/L})$$

$$\text{VAI} = \frac{\text{WC}(\text{cm})}{36.58 + 1.89 \times \text{BMI}(\text{kg/m}^2)} \times \frac{\text{TG}(\text{mmol/L})}{0.81} \times \frac{1.52}{\text{HDL-C}(\text{mmol/L})}$$

WC (cm), TG (mmol/L), HDL-C (mmol/L) and BMI (kg/m^2) were derived from NHANES measurements.

Definition of EMS

The diagnosis of EMS was based on participants' responses to the Reproductive Health Questionnaire (RHQ).¹⁵ Specifically, participants were asked, "Has a doctor ever told you that you had endometriosis?" Those who answered "yes" were classified as EMS cases, while those who answered "no" were classified as non-EMS.

Covariates

Covariates were selected based on prior literature^{3,12,13,16} and included: age, race/ethnicity, education level, poverty income ratio (PIR), smoking status, alcohol consumption, hypertension, diabetes, age at menarche, uterine fibroids and history of oral contraceptive use. Detailed definitions of covariates are provided in Supplementary Table S1.

Statistical analysis

All statistical analyses accounted for NHANES's complex sampling design, using fasting subsample weights, SDMVSTRA and SDMVPSU. Continuous variables were presented as means (95% confidence interval [CI]), and categorical variables were presented as percentages (95% CI). Because LAP and VAI were

skewed, Log_2 transformations (Log_2 LAP and Log_2 VAI) were applied to correct for data skewness. Participants were divided into 2 groups based on EMS status, and group differences were assessed using t-tests and chi-square tests. Logistic regression models were employed to evaluate the associations between Log_2 LAP, Log_2 VAI and EMS, using 3 models: Model 1 (unadjusted), Model 2 (adjusted for age, race/ethnicity, marital status and PIR) and Model 3 (adjusted for all covariates). Smoothed curve fitting and generalised additive models were used to visualise the linear relationships between Log_2 LAP, Log_2 VAI and EMS. Subgroup analyses and interaction tests were conducted to explore the potential modifying effects of age, hypertension, diabetes, smoking, alcohol consumption, age at menarche, uterine fibroids and oral contraceptive use. A 2-tailed P value was considered statistically significant if less than 0.05. All analyses were performed using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) and Empower (X&Y Solutions Inc, MA, US).

RESULTS

Baseline characteristics of participants

This study included 2046 participants, of whom 161 were diagnosed with EMS. Table 1 presents the baseline characteristics of the study population. Compared to the non-EMS group, EMS participants were older and had higher TG levels. The EMS group also showed significantly higher Log_2 LAP and Log_2 VAI values (all $P < 0.05$). There were differences in racial/ethnic distribution, with a higher proportion of non-Hispanic, White individuals in the EMS group. Additionally, significant differences were observed between the 2 groups regarding marital status, presence of uterine fibroids, oral contraceptive use and smoking status (all $P < 0.05$). However, no significant differences were observed between the groups in PIR, BMI, WC, HDL-C, diabetes status or age at menarche (all $P > 0.05$).

Associations between Log_2 LAP, Log_2 VAI and EMS

Table 2 presents the logistic regression analysis results for the associations between Log_2 LAP, Log_2 VAI, their quartiles and the risk of EMS.

In Model 1, Log_2 LAP was significantly associated with an increased risk of EMS (OR 1.327, 95% CI 1.149–1.532). This association remained significant in Model 2 (OR 1.314, 95% CI 1.144–1.508, $P=0.0003$). Even after full adjustment in Model 3, the association between Log_2 LAP and EMS remained robust and significant (OR 1.256, 95% CI 1.102–1.431, $P=0.0014$). When analysed by quartiles, compared to the Q1 group, the ORs (95% CIs) for EMS in Q2,

Table 1. Baseline characteristics of participants according to EMS.

Characteristics	Total	Without EMS (n=1885)	With EMS (n=161)	P value
Age, years (95% CI)	37.55 (36.96–38.15)	37.25 (36.61–37.89)	40.12 (38.90–41.34)	0.0001
PIR, ratio (95% CI)	3.02 (2.92–3.13)	3.01 (2.90–3.11)	3.18 (2.86–3.51)	0.3088
BMI, kg/m ² (95% CI)	28.08 (27.67–28.48)	28.04 (27.61–28.47)	28.40 (27.41–29.39)	0.5061
WC, cm (95% CI)	92.18 (91.26–93.10)	91.98 (91.01–92.94)	93.97 (91.47–96.47)	0.1378
TG, mmol/L (95% CI)	1.38 (1.31–1.44)	1.32 (1.27–1.37)	1.91 (1.46–2.36)	0.0139
HDLC, mmol/L (95% CI)	1.48 (1.46–1.50)	1.48 (1.46–1.51)	1.45 (1.37–1.54)	0.4784
Log ₂ LAP, (95% CI)	5.14 (5.07–5.20)	5.09 (5.01–5.16)	5.54 (5.33–5.75)	0.0004
Log ₂ VAI, (95% CI)	0.64 (0.59–0.70)	0.60 (0.54–0.66)	0.99 (0.81–1.17)	0.0003
Race, % (95% CI)				<0.0001
Mexican American	7.51 (6.13–9.16)	8.21 (6.71–10.02)	1.42 (0.65–3.05)	
Other Hispanic	5.12 (3.35–7.75)	5.49 (3.53–8.43)	1.96 (0.68–5.54)	
Non-Hispanic White	70.40 (67.07–73.53)	68.75 (65.12–72.16)	84.66 (78.87–89.08)	
Non-Hispanic Black	11.84 (9.81–14.22)	12.28 (10.11–14.83)	8.05 (5.66–11.35)	
Other Race	5.13 (3.83–6.84)	5.27 (3.96–7.00)	3.90 (1.55–9.51)	
Marriage, % (95% CI)				0.0425
Married/living with a partner	68.11 (65.58–70.55)	67.32 (64.54–69.99)	74.92 (65.42–82.51)	
Divorced/separated/widowed	14.92 (13.08–16.97)	14.76 (12.84–16.91)	16.31 (9.56–26.44)	
Never married	16.97 (14.77–19.41)	17.92 (15.57–20.54)	8.77 (5.42–13.88)	
Drink, % (95% CI)				0.6160
Yes	68.14 (64.06–71.96)	67.87 (63.81–71.68)	70.46 (58.82–79.93)	
No	31.86 (28.04–35.94)	32.13 (28.32–36.19)	29.54 (20.07–41.18)	
Hypertension, % (95% CI)				0.4688
Yes	19.12 (16.85–21.61)	18.89 (16.52–21.51)	21.12 (15.54–28.04)	
No	80.88 (78.39–83.15)	81.11 (78.49–83.48)	78.88 (71.96–84.46)	

Table 1. Baseline characteristics of participants according to EMS. (Cont'd)

Characteristics	Total	Without EMS (n=1885)	With EMS (Total=161)	P value
Diabetes, % (95% CI)				0.6250
Yes	3.88 (2.89–5.19)	3.96 (2.94–5.31)	3.20 (1.29–7.73)	
No	96.12 (94.81–97.11)	96.04 (94.69–97.06)	96.80 (92.27–98.71)	
Age of menarche, % (95% CI)				0.1638
<13 years	49.53 (46.38–52.68)	48.75 (45.61–51.89)	56.28 (45.33–66.65)	
≥13 years	50.47 (47.32–53.62)	51.25 (48.11–54.39)	43.72 (33.35–54.67)	
Uterine fibroids, % (95% CI)				<0.0001
Yes	15.36 (13.45–17.49)	13.17 (11.47–15.07)	34.23 (27.08–42.18)	
No	84.64 (82.51–86.55)	86.83 (84.93–88.53)	65.77 (57.82–72.92)	
History of oral contraceptive pill use, % (95% CI)				0.0040
Yes	81.03 (78.19–83.59)	79.88 (76.70–82.72)	90.98 (84.14–95.05)	
No	18.97 (16.41–21.81)	20.12 (17.28–23.30)	9.02 (4.95–15.86)	
Smoke, % (95% CI)				<0.0001
Yes	42.48 (39.22–45.81)	40.44 (36.95–44.03)	60.01 (51.22–68.19)	
No	57.52 (54.19–60.78)	59.56 (55.97–63.05)	39.99 (31.81–48.78)	

BMI: body mass index; CI: confidence interval; EMS: endometriosis; HDL-C: high-density lipoprotein cholesterol; LAP: lipid accumulation product; PIR: poverty income ratio; TG: triglycerides; VAI: visceral adiposity index; WC: waist circumference

Q3 and Q4 were 1.397 (0.758–2.576), 1.499 (0.854–2.630) and 1.983 (1.299–3.028), respectively, with a significant dose-response trend (P for trend=0.0022).

Similarly, Log_2 VAI was positively associated with EMS in Model 1 (OR 1.403, 95% CI 1.207–1.631), Model 2 (OR 1.385, 95% CI 1.194–1.607) and Model 3 (OR 1.287, 95% CI 1.105–1.498). When analysed by quartiles in Model 3, compared to the Q1 group, the ORs (95% CIs) for EMS in Q2, Q3 and Q4 were 1.188 (0.692–2.039), 1.398 (0.832–2.348) and 1.690 (1.019–2.803), respectively. The risk in the Q4 group was significantly increased ($P=0.0486$) and a significant trend was observed (P for trend=0.0307).

The smoothed curve fitting plots further showed that, after adjusting for all covariates, Log_2 LAP and

Log_2 VAI were linearly and positively associated with EMS (Fig. 2).

Subgroup analysis

To explore heterogeneity across subgroups, we performed subgroup analyses and interaction tests (Fig. 3). Significant positive associations with EMS were observed in women aged ≥35 years, those without hypertension, smokers, drinkers, those without a history of uterine fibroids, and those with a history of oral contraceptive use. For subgroups defined by age at menarche, associations were significant in both, but no significant interaction was observed (Fig. 3A). For diabetic status, associations were significant in both diabetic and non-diabetic participants, with a statistically significant interaction

Table 2. The relationship between Log₂ LAP and Log₂ VAI and EMS.

	Model 1 OR (95% CI) P value	Model 2 OR (95% CI) P value	Model 3 OR (95% CI) P value
Log₂ LAP	1.327 (1.149–1.532) 0.0003	1.314 (1.144–1.508) 0.0003	1.256 (1.102–1.431) 0.0014
Log₂ LAP quartiles			
Q1 -2.00 to 4.44	Ref	Ref	Ref
Q2 4.44 to 5.35	1.412 (0.767–2.599) 0.2720	1.437 (0.787–2.626) 0.2440	1.397 (0.758–2.576) 0.2904
Q3 5.35 to 6.29	1.512 (0.836–2.732) 0.1766	1.519 (0.836–2.761) 0.1762	1.499 (0.854–2.630) 0.1660
Q4 6.29 to 9.52	2.374 (1.466–3.845) 0.0009	2.320 (1.451–3.709) 0.0010	1.983 (1.299–3.028) 0.0029
P for trend	0.0007	0.0006	0.0022
Log₂ VAI	1.403 (1.207–1.631) <0.0001	1.385 (1.194–1.607) 0.0001	1.287 (1.105–1.498) 0.0022
Log₂ VAI quartiles			
Q1 -2.10 to -0.04	Ref	Ref	Ref
Q2 -0.04 to 0.70	1.255 (0.744–2.118) 0.3988	1.226 (0.721–2.083) 0.4552	1.188 (0.692–2.039) 0.5352
Q3 0.70 to 1.42	1.616 (0.961–2.717) 0.0754	1.608 (0.959–2.694) 0.0778	1.398 (0.832–2.348) 0.2132
Q4 1.42 to 5.70	2.064 (1.221–3.490) 0.0090	2.001 (1.186–3.374) 0.0123	1.690 (1.019–2.803) 0.0486
P for trend	0.0040	0.0044	0.0307

Model 1: Unadjusted

Model 2: Adjusted for age, race/ethnicity, marital status and PIR

Model 3: Adjusted for age, race/ethnicity, marital status, PIR, hypertension, diabetes, smoking status, alcohol consumption, age at menarche, uterine fibroids and history of oral contraceptive use.

CI: confidence interval; EMS: endometriosis; OR: odds ratio; LAP: lipid accumulation product; OR: odds ratio; VAI: visceral adiposity index

(*P* for interaction=0.023), suggesting potential effect modification by diabetes. However, due to the smaller sample size in the diabetic subgroup, estimates should be interpreted with caution.

Significant positive associations with EMS were observed in women aged ≥35 years, those without hypertension, smokers, non-drinkers, those with age at menarche ≥13 years, those without uterine fibroids, and those with a history of oral contraceptive use (Fig. 3B). For diabetic status, associations were significant in both diabetic and non-diabetic participants; however, no significant interaction was observed (*P* for interaction=0.067).

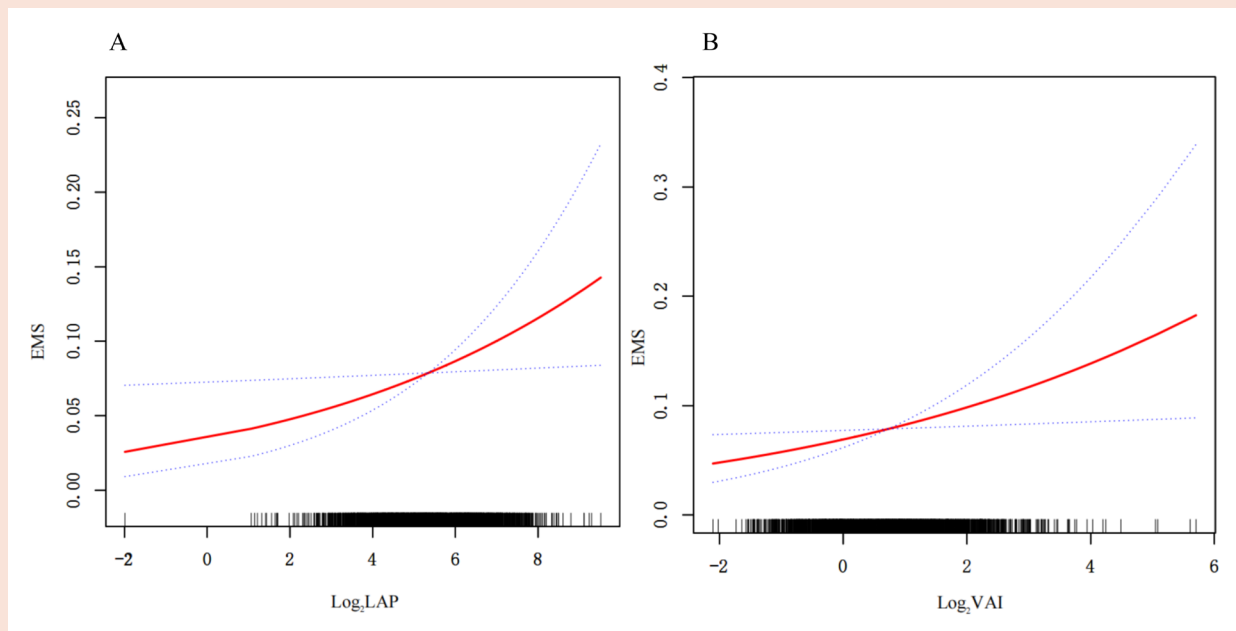
DISCUSSION

This study systematically evaluated the associations between 2 composite indicators of visceral obesity

and lipid metabolic disturbances—LAP and VAI—and the risk of EMS. Our findings showed that, after adjusting for multiple potential confounders, higher levels of both LAP and VAI were independently associated with increased prevalence of endometriosis. Women in the highest LAP quartile had nearly twice the risk of EMS compared to those in the lowest quartile, and a similar positive trend was observed across VAI quartiles.

Our results align with recent studies investigating other metabolic markers and EMS. Wang et al.³ reported that a higher cardiometabolic index (CMI) was significantly associated with an increased risk of EMS. Similarly, a study on the triglyceride-glucose (TyG) index, a surrogate marker of insulin resistance, found that EMS prevalence increased with higher TyG levels.¹⁶ Multiple studies have highlighted a

Fig. 2. Smooth curve fitting of the associations between Log_2 LAP, Log_2 VAI and EMS, adjusted for covariates in Model 3. (A) Log_2 LAP and EMS; (B) Log_2 VAI and EMS.



EMS: endometriosis, LAP: lipid accumulation product; VAI: visceral adiposity index

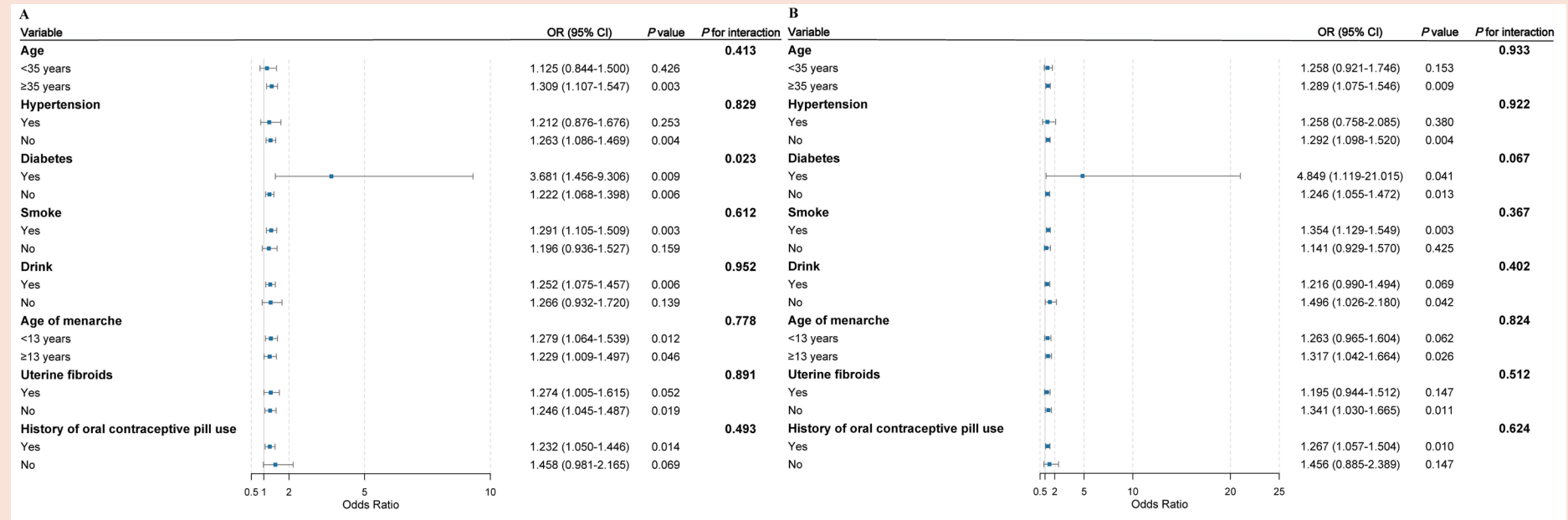
significant association between lipid metabolic abnormalities and EMS, with EMS patients more prone to lipid metabolism disorder.^{13,17,18} Unlike single biomarkers such as TyG or CMI, which primarily reflect insulin resistance or specific lipid components, LAP and VAI integrate visceral obesity and lipid dysfunction, offering a more comprehensive reflection of the metabolic networks underlying EMS. By combining anthropometric measures with lipid profiles, LAP and VAI capture the synergistic effects of visceral fat accumulation and dyslipidaemia, which may more accurately represent the multifaceted metabolic disturbances driving EMS pathogenesis.¹⁹

Our study demonstrates that elevated LAP and VAI are linked to an increased risk of EMS, which may involve several key pathophysiological mechanisms. EMS is characterised by chronic inflammation, which is not confined to the pelvic cavity but extends to systemic inflammatory responses.¹ Visceral adipose tissue is a major source of pro-inflammatory cytokines, which are significantly elevated in the peritoneal fluid of EMS patients.²⁰ As indicators of visceral fat accumulation, LAP and VAI may reflect an enhanced pro-inflammatory environment that promotes the adhesion, proliferation and angiogenesis of ectopic endometrial cells, thereby exacerbating the pathological processes of EMS.²¹ Additionally, LAP and VAI are closely related to insulin resistance, the core feature of metabolic syndrome. IR-induced hyperinsulinaemia can affect EMS development through

multiple pathways.²² IR also alters hormone levels by reducing sex hormone-binding globulin, thereby increasing circulating androgens and free oestrogens, upregulating phosphorylated forkhead box O1 in ectopic stromal cells, and enhancing the expression of Ras-related proteins and matrix metalloproteinase-9, which together increase the invasiveness of EMS.¹⁶ This insulin-driven hormonal dysregulation may amplify oestrogen-dependent growth of ectopic lesions, further linking LAP and VAI to EMS pathogenesis.

Visceral adipose tissue is also a key site for peripheral oestrogen production through aromatisation of androgens.²³ Elevated LAP and VAI may lead to increased systemic oestrogen levels, providing a favourable hormonal environment for the growth of oestrogen-dependent EMS lesions. Moreover, dyslipidaemia associated with visceral obesity may disrupt hormonal metabolic balance, further exacerbating hormonal dysregulation in EMS. Visceral fat accumulation and metabolic syndrome are also linked to increased systemic oxidative stress, which is another hallmark of EMS.²⁴ Reactive oxygen species can promote the formation and maintenance of ectopic lesions by damaging cellular components, inducing inflammation and stimulating angiogenesis.²⁵ Individuals with elevated LAP and VAI may face a higher oxidative stress burden, which, combined with the intrinsic oxidative imbalance of EMS, drives disease progression. Finally, metabolic abnormalities driven by visceral fat may impair immune surveillance,

Fig. 3. Forest plot of subgroup analysis for relationships between Log₂ LAP and Log₂ VAI and EMS. (A) Forest plot of subgroup analysis for relationships between Log₂ LAP and EMS; (B) Forest plot of subgroup analysis for relationships between Log₂ VAI and EMS.



CI: confidence interval; EMS: endometriosis; LAP: lipid accumulation product; OR: odds ratio; VAI: visceral adiposity index

while EMS itself has been shown to involve immune dysfunction, including altered macrophage polarisation, reduced natural killer cell cytotoxicity, and shifts in T cell populations.^{26–28} The inflammatory environment triggered by excess visceral fat may amplify these immune defects, allowing ectopic endometrial cells to evade immune clearance and establish lesions.

Our subgroup analyses showed that the associations between LAP, VAI and EMS were statistically significant across many subgroups. As women age, oestrogen levels gradually decline, and oestrogen plays a key role in regulating fat distribution and metabolism.^{2,29} Reduced oestrogen may lead to increased visceral fat accumulation, thereby exacerbating metabolic disturbances.³⁰ A cross-sectional study based on NHANES data found a positive association between LAP and EMS prevalence, particularly in women aged 35 years and older,³¹ suggesting that age-related hormonal changes may amplify the associations between LAP, VAI and EMS. In addition, ageing is often accompanied by heightened chronic inflammation, which may further promote the development of EMS.³² Alcohol consumption may influence the association between VAI and EMS by modulating lipid metabolism and visceral fat accumulation. One study found that moderate alcohol intake was associated with improved insulin sensitivity and reduced inflammation,³³ which could weaken the impact of VAI as a metabolic abnormality indicator on EMS. Moreover, alcohol metabolism may interfere with hormonal balance (e.g. oestrogen metabolism), thereby dampening the association between VAI and EMS.³⁴ In contrast, among non-drinkers, the lack of this regulatory mechanism may make the relationship between VAI, visceral adiposity and metabolic risk more directly linked to EMS.

The subgroups without hypertension may represent metabolically healthier populations, where LAP and VAI primarily reflect visceral fat accumulation¹⁰ rather than the influence of comorbidities, thus showing a more direct association with EMS. For smokers, smoking may enhance the associations between LAP, VAI and EMS by inducing chronic inflammation or affecting hormone metabolism. Studies have shown that smoking is associated with an increased risk of EMS, which may amplify the effects of metabolic disturbances.³⁵ Later age at menarche may be related to a longer period of low oestrogen exposure, influencing fat distribution and metabolic status, thereby strengthening the associations between LAP, VAI and EMS. Additionally, the absence of uterine fibroids and a history of oral contraceptive use may reflect differences in hormonal status or reproductive health. Oral contraceptives, by modulating hormone levels, may indirectly affect metabolism and EMS

risk, though the exact mechanisms warrant further investigation.

Notably, the associations of LAP and VAI with EMS were more pronounced in the diabetes subgroup than in the non-diabetes subgroup. Diabetes and its related insulin resistance may serve as effect modifiers in the relationship between LAP and EMS, as well as between VAI and EMS. Patients with diabetes are typically characterised by systemic metabolic disturbances, hyperinsulinemia and chronic low-grade inflammation, all of which may exacerbate visceral fat accumulation, enhance the release of pro-inflammatory cytokines, and promote insulin-driven hormonal imbalances that stimulate ectopic endometrial proliferation. Together with oxidative stress and immune dysfunction, these processes may synergistically amplify the impact of LAP and VAI on EMS risk.^{36,37} Nevertheless, the relatively small sample size of the diabetes subgroup, along with the wide confidence intervals—particularly for VAI—necessitates cautious interpretation. Future large-scale prospective studies are warranted to confirm whether diabetes truly modifies the associations of LAP and VAI with EMS and to further elucidate the underlying metabolic and inflammatory mechanisms.

Clinical implications

The findings of this study have potential clinical relevance. LAP and VAI can be easily calculated using routine anthropometric measurements and lipid profiles, making them practical tools for EMS risk assessment. For women with elevated LAP or VAI, especially those with metabolic conditions such as diabetes, clinicians can incorporate these indices into routine health assessments to identify individuals at higher risk for EMS, facilitating early screening and intervention. Furthermore, lifestyle interventions, such as dietary modifications and increased physical activity to reduce visceral fat, may serve as complementary strategies to prevent or manage EMS and improve metabolic health. Given the cross-sectional design and reliance on self-reported EMS, LAP and VAI are currently best suited to identify high-risk populations for further clinical evaluation rather than as diagnostic tools.

Limitations

Despite providing valuable insights, this study has several limitations. First, the cross-sectional design precludes causal inference, and the complex pathophysiology of EMS may influence the interpretation of metabolic parameters. EMS diagnosis was based on self-reporting, which may lead to underdiagnosis or misclassification, introducing recall bias and potentially affecting the observed associations between LAP, VAI and EMS. Furthermore,

the study population was limited to women in the US, restricting the generalisability of the findings. Although multiple confounders were adjusted for, some unmeasured factors may still have influenced the results, including common hormonal treatments for EMS, dietary patterns and physical activity levels. Hormonal treatments can substantially alter metabolic parameters, such as lipid profiles, while high-fat or high-sugar diets may exacerbate visceral fat accumulation and systemic inflammation, and regular physical activity may mitigate metabolic dysfunction. These factors could collectively affect the associations between LAP, VAI and EMS, and warrant further investigation in future studies. Although subgroup analyses revealed intriguing patterns, particularly stronger associations among diabetic women, the relatively small number of EMS cases limited statistical power. Therefore, these subgroup findings should be interpreted cautiously and validated in larger, adequately powered cohorts. Future research should employ prospective cohort designs; incorporate precise clinical diagnoses; include a broader range of metabolic markers; and account for treatment interventions to validate the potential of LAP and VAI as predictive markers for EMS.

CONCLUSION

This study demonstrates a significant association between LAP, VAI and EMS prevalence, highlighting their potential as metabolic markers for risk assessment. Prospective cohort studies with clinical EMS diagnoses are needed to clarify causality and evaluate the utility of LAP and VAI in EMS management.

Supplementary material

Supplementary Table S1. Definition of covariates.

Ethics

Ethical approval was not required for this study as it used publicly available, anonymised data from the US National Health and Nutrition Examination Survey.

Declaration

This study received funding from the National Natural Science Foundation (No.82474566) and the Key Research and Development Program Project of Heilongjiang Province (No.2024ZX12C25). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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