

Latent Class Characteristics and Influencing Factors of Allostatic Load Among Pregnant Women

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Abstract

Background Allostatic load (AL), as a comprehensive indicator of multisystem physiological dysregulation under chronic stress, is associated with multiple influencing factors. However, most existing studies employ a total-score dichotomization approach, neglecting the heterogeneity of physiological dysregulation patterns across individuals, which hinders the development of precision health management during pregnancy. **Objective** To identify latent subgroups of AL among pregnant women based on eight biomarkers, analyze the sociodemographic characteristics, psychological factors, and lifestyle behaviors associated with different AL latent classes, and provide scientific evidence for community- and obstetrics-based stratified precision health management.

Methods This study presents a secondary analysis of data from a prospective cohort study. A convenience sampling method was used to recruit 850 singleton pregnant women in their second or third trimester from two tertiary hospitals in Anhui Province between November 2021 and November 2023. Eight AL indicators were extracted from the original dataset, including systolic blood pressure, diastolic blood pressure, BMI, waist circumference, total cholesterol, high-density lipoprotein, fasting blood glucose, and high-sensitivity C-reactive protein. The high-risk quartile method was used for dichotomous scoring and summation. Latent class analysis (LCA) was performed to identify AL subtypes. Chi-square tests and Kruskal-Wallis tests were used to compare sociodemographic characteristics, psychological factors, and behavioral characteristics across classes. Multinomial logistic regression was used to identify independent influencing factors for each class, with Class 4 (multisystem combined high-load group) among the four latent classes as the reference.

Results A four-class model best fit the data: ① Low-load group (11.6%), with the lowest risk levels across all eight indicators; ② Metabolic high-load group (8.5%), characterized by high risks in metabolic indicators (waist circumference, BMI, fasting blood glucose) and low cardiovascular risks; ③ Cardiovascular-metabolic high-load group (19.4%), with high risks in both cardiovascular and metabolic indicators; ④ Multisystem combined high-load group (60.5%), with the highest risk levels across all eight indicators. Univariate analysis showed significant differences among the four classes in gestational week, adverse pregnancy history, and anxiety ($P < 0.05$). Using Class 4 as the reference, multinomial logistic regression revealed that anxiety was an independent influencing factor for AL class membership. Pregnant women without anxiety had significantly higher risks of being classified into Class 1, Class 2, and Class 3 (OR=2.243–2.570, all $P < 0.05$), indicating that anxious pregnant women were more likely to be classified into the multisystem combined high-load group.

Conclusion AL among pregnant women exhibits significant population heterogeneity and can be classified into four distinct physiological dysregulation subtypes, with the multisystem combined high-load group accounting for the largest proportion (60.5%). Anxiety is a key factor distinguishing these AL subtypes. Community health workers and obstetric care providers are advised to implement stratified precision interventions based on the physiological characteristics of each subtype, in order to mitigate the adverse health effects of chronic stress on both mothers and offspring.

Trial registration : The original cohort study was registered in the Chinese Clinical Trial Registry (ChiCTR2200066044), registered on 22 November 2022.

Introduction

Allostatic load (AL) refers to the cumulative physiological “wear and tear” induced by chronic stress exposure^[1]. Originally conceptualized by McEwen and Stellar in 1993^[2], it describes the cumulative biological burden borne by the neuroendocrine, immune, cardiovascular, and metabolic systems in response to repeated or sustained environmental challenges. AL reflects not only the additive effects of daily stressors and major life events, but also the physiological consequences of health-compromising behaviors^[1]. As a composite measure of multisystem physiological dysregulation under chronic stress, AL reliably predicts a wide range of adverse health outcomes. Pregnancy represents a period of profound physiological and psychological stress across a woman’s reproductive lifespan. During pregnancy, the maternal neuroendocrine, immune, cardiovascular, and metabolic systems undergo extensive remodeling and adaptive changes to support fetal growth and development^[3]. However, persistent chronic stress may drive excessive activation or dysregulation of these systems, resulting in elevated AL levels. In recent years, research on AL in pregnancy has received growing attention. Evidence indicates that high gestational AL is closely associated with multiple adverse pregnancy outcomes^[4].

One study^[5] demonstrated that AL scores were significantly and positively correlated with spontaneous preterm birth risk: women in the high-AL group had a 2.09-fold higher risk than those in the low-AL group. Another study showed that high AL in late pregnancy represents a risk factor for preterm birth and macrosomia^[6]. Additionally, gestational AL has been linked to hypertensive disorders of pregnancy, sleep-disordered breathing, delayed lactogenesis onset, and long-term risk of obesity and insulin resistance in offspring^{[7–}

^{10]}. Psychologically, gestational AL is also closely associated with mental health outcomes, including depression^[11]. A prospective study

of Chinese pregnant women reported that the prevalence of high AL was 34.2%, 35.5%, and 32.9% in the first, second, and third trimesters, respectively, with over 30% of women exhibiting high AL at different gestational stages^[12]. This finding highlights the substantial public health relevance of AL in pregnant populations. However, most prior studies^[13, 14] have categorized AL into binary high/low levels based on total scores. This dichotomous approach obscures heterogeneity in physiological dysregulation patterns across individuals, as pregnant women may present distinct combinations of dysregulated physiological systems.

Latent class analysis (LCA), a person-centered analytical method, groups individuals into latent subgroups based on their response profiles across multiple indicators, thereby revealing underlying population heterogeneity^[15]. LCA has been applied to identify latent AL classes among pregnant populations. A study applied LCA to preconception AL biomarkers in non-Hispanic White women and identified four distinct classes, including a hypertension class and a class with elevated BMI and waist circumference, with divergent associations with adverse birth outcomes across classes^[16]. Molenaar et al. used preconception data to identify vulnerable subgroups of pregnant women via LCA, offering a novel framework for prenatal risk stratification^[17]. These findings suggest that distinct AL subtypes may exert differential effects on pregnancy outcomes, and that relying solely on total AL scores may fail to capture critical heterogeneity. Zhou et al.^[5] identified three latent classes of AL in second-trimester pregnant women from a Chinese cohort: the low dysregulation group, the metabolic-immune dysregulation group, and the cardiovascular dysregulation group, of which the metabolic-immune dysregulation group was significantly associated with spontaneous preterm birth risk. Nevertheless, research on latent AL classes in pregnant women remains limited, particularly with a lack of systematic analyses across multiple gestational time points, and the correlates of AL class membership remain poorly understood.

Therefore, this study enrolled pregnant women in both the second and third trimesters and incorporated anxiety and depression scales. Using latent class analysis (LCA), this study aimed to characterize the latent profile of AL among pregnant women, identify distinct AL subtypes and their distribution across pregnancy, and explore influencing factors associated with AL latent-class membership. The findings can provide scientific evidence for individualized antenatal care services, and also facilitate the early identification of high-risk populations and the formulation of targeted intervention strategies.

1 Materials and Methods

1.1 Study participants

This study presents a secondary analysis of data from a large-sample cross-sectional data study previously conducted by our research group. Participants were recruited via convenience sampling from the obstetric outpatient clinics of two tertiary hospitals in Hefei and Lu'an, China, Anhui Province, between November 2021 and November 2023. Data analysis and sorting were performed from July to August 2026. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) natural conception and singleton pregnancy; (3) received routine antenatal care and planned to deliver at the study hospitals; (4) cognitively intact and able to communicate effectively; (5) provided written informed consent. The exclusion criteria were as follows: (1) pre-pregnancy chronic medical conditions, including heart disease, hypertension, and diabetes mellitus; (2) history of severe mental illness. Ultimately, a total of 850 women in the second trimester (23–27 weeks) and third trimester (30–34 weeks) were included in the final analysis.

1.2 Data collection

Data were collected at two scheduled follow-up visits: the second trimester (23–27 gestational weeks) and the third trimester (30–34 gestational weeks). The dataset covered four domains: sociodemographic and clinical characteristics, allostatic load biomarkers, psychological status, and lifestyle behaviors.

1.2.1 Allostatic load parameters

Consistent with previous studies^[18,19], eight biomarkers were used to assess allostatic load. Anthropometric measurements included systolic blood pressure, diastolic blood pressure, height, weight, and waist circumference; body mass index (BMI) was calculated accordingly. Fasting venous blood samples were collected to measure total cholesterol, high-density lipoprotein cholesterol, fasting blood glucose, and high-sensitivity C-reactive protein (hs-CRP). Specifically, metabolic markers included high-density lipoprotein cholesterol, total cholesterol, BMI, fasting blood glucose, and waist circumference; cardiovascular markers included systolic and diastolic blood pressure; the immune marker was represented by hs-CRP. Data of above biomarkers were extracted from the original prospective cohort dataset. The high-risk quartile method was applied to score each AL biomarker. For high-density lipoprotein cholesterol, the lower quartile was defined as high risk; for all other biomarkers, the upper quartile was used as the high-risk cutoff. Detailed cutoff values are presented

in Table 1. Each biomarker was assigned a score of 1 for high risk and 0 for low risk. Individual scores were summed to generate a total AL score. Consistent with existing literature, a total AL score ≥ 3 was defined as the threshold for high AL [20].

Table 1 Risk Quartile Cutoffs for Allostatic Load

Biological indicator	Cutoff value
Waist circumference (cm)	≥ 101.000
Systolic blood pressure (mmHg)	≥ 122.000
Diastolic blood pressure (mmHg)	≥ 78.000
BMI (kg/m ²)	≥ 27.640
Total cholesterol (mmol/L)	≥ 6.670
High-sensitivity C-reactive protein (mg/L)	≥ 3.630
Fasting blood glucose (mmol/L)	≥ 5.100
High-density lipoprotein (mmol/L)	≤ 1.540

1.2.2 Independent variables

The independent variables in this study fell into three domains: sociodemographic characteristics, psychological factors, and lifestyle behaviors.

1) Sociodemographic characteristics: age, gestational week, educational level, occupation, history of adverse pregnancy outcomes, and pregnancy complications. 2) Psychological factors: anxiety status and depressive symptoms. 3) Lifestyle behaviors: history of alcohol use and physical activity level. Pregnancy-related anxiety, depressive symptoms, and physical activity were assessed using the Chinese version of the Pregnancy-Related Anxiety Questionnaire (PRAQ) [21], the Edinburgh Postnatal Depression Scale (EPDS) [22], and the International Physical Activity Questionnaire-Short Form (IPAQ-S) [23], respectively. The PRAQ consists of 13 items with a total score ranging from 13 to 52; a cutoff score of ≥ 24 was applied to define the presence of pregnancy-related anxiety. The Cronbach's α coefficient of the Chinese PRAQ in the present sample was 0.89. The EPDS comprises 10 items with a total score ranging from 0 to 30; a score ≥ 9 was considered indicative of depressive mood, with a Cronbach's α of 0.718 in this study. Based on weekly total metabolic equivalent minutes (MET-min/week), physical activity levels derived from the IPAQ-S were classified into three tiers: low (< 600 MET-min/week), moderate (600–3000 MET-min/week), and high (≥ 3000 MET-min/week).

1.3 Statistical methods

Data extraction and statistical analyses were performed using SPSS version 27.0 and Mplus version 8.7. Normally distributed continuous variables are expressed as mean $\pm$ standard deviation, non-normally distributed continuous variables as median (interquartile range), and categorical variables as frequencies and percentages (%). Between-group comparisons were conducted using chi-square tests for categorical variables, analysis of variance (ANOVA) for normally distributed continuous variables, and Kruskal–Wallis tests for non-normally distributed continuous variables. Latent class analysis of allostatic load was conducted using Mplus 8.7, with the following model fit indices evaluated: log-likelihood (LL), Akaike information criterion (AIC), Bayesian information criterion (BIC), sample-size adjusted Bayesian information criterion (aBIC), entropy, Lo-Mendell-Rubin adjusted likelihood ratio test (LMR), and Bootstrap likelihood ratio test (BLRT). Lower values of AIC, BIC, and aBIC indicated better model fit, while a larger LL value corresponded to improved fit. Entropy values closer to 1.0 indicated better classification accuracy, with an entropy value of approximately 0.8 corresponding to a classification accuracy of over 90%. For LMR and BLRT, a P -value < 0.05 indicated that the k -class model fit significantly better than the $(k-1)$ -class model. Model selection was based primarily on the lowest BIC value and statistically significant BLRT results as core criteria [24], with clinical interpretability also taken into consideration. Once the optimal number of classes was determined, variables showing statistical significance in univariable analysis were entered into a multinomial logistic regression model, with Class 4 (multisystem combined high-load group) as the reference category, to identify factors independently associated with membership in the other three latent classes. The significance level was set at $\alpha = 0.05$ (two-sided).

1.4 Ethical approval

The original prospective cohort study was approved by the Ethics Committee of Anhui Medical University (approval number: s20210076) and registered in the Chinese Clinical Trial Registry (ChiCTR2200066044) on 22 November 2022. All participants provided written informed consent. The original cohort study was conducted in accordance with the principles of the Declaration of Helsinki. As the present study is a secondary analysis of de-identified existing data and does not involve direct intervention involving human subjects, it was deemed exempt from further institutional review board review.

1.5 Quality control

This study performed a secondary analysis by extracting the required data from a previously established cross-sectional database of pregnant women. In the original study, investigators and testing personnel were uniformly trained, and standardized procedures were implemented for physical measurements, blood sampling, and laboratory testing. Data were double-entered and logically cross-checked, and inclusion and exclusion criteria were strictly applied. In this secondary analysis, the required variables were extracted, and samples with missing core AL indicators were excluded. Risk assignment rules for each indicator were standardized, and categorical variables were consistently coded. In LCA modeling, multiple random start values were set to prevent local optima, and all statistical results and figures were repeatedly cross-checked to ensure the reliability and validity of the analytical results.

2 Results

2.1 Latent classes of allostatic load among pregnant women

Model fit improved progressively as the number of latent classes increased, as reflected by continuous declines in AIC and aBIC values. The 4-class model demonstrated relatively low AIC (7011.942) and aBIC (7066.876), with an entropy of 0.932 indicating excellent classification accuracy. The smallest class represented 8.5% of the total sample, with a sufficient sample size to support robust subgroup analysis. For the 4-class model, the *P*-values of the LMR and BLRT tests were both > 0.05, indicating that the 4-class solution did not fit statistically better than the 3-class solution. For the 5-class and 6-class models, the reduction in AIC was negligible, whereas BIC values increased and entropy values decreased, providing no additional statistical or clinical utility. Taking into account model fit indices, classification accuracy, class size distribution, and the clinical interpretability of the four distinct physiological profiles, the 4-class model was ultimately determined as the optimal solution. Detailed model fit indices for all latent class solutions are summarized in Table 2.

Table 2 Model Fit Indices of Latent Class Model for Allostatic Load Among Pregnant Women

Classes	LL	AIC	BIC	aBIC	Entropy	LMR [P]	BLRT [P]	Class probabilities
1	-3786.476	7588.952	7626.914	7601.509				
2	-3543.601	7121.201	7201.870	7147.883	0.803	0.001	0.0001	0.695/0.305
3	-3488.860	7029.719	7153.096	7070.527	0.737	0.6747	0.931	0.128/0.273/0.599
4	-3470.971	7011.942	7178.025	7066.876	0.932	0.9556	0.967	0.605/0.116/0.085/0.194
5	-3459.000	7006.000	7214.791	7075.060	0.888	0.9949	0.9969	0.169/0.125/0.109/0.416/0.180
6	-3448.187	7002.375	7253.872	7085.560	0.901	0.9975	0.9998	0.107/0.156/0.153/0.033/0.373/0.178

2.2 Naming and characteristics of the latent classes of allostatic load among pregnant women

Based on the conditional probability distribution of the eight indicators across each class, the four latent classes were named as follows: Class 1: Low-load group (11.6%, n = 99). Pregnant women in this group had the lowest high-risk probabilities across all eight indicators, reflecting a very low cumulative chronic stress burden and representing the ideal subgroup with the least physiological wear and tear. Class 2: Metabolic high-load group (8.5%, n = 72). This group was characterized by prominent metabolic abnormalities, with waist circumference, BMI, high-sensitivity C-reactive protein, fasting blood glucose, and total cholesterol all at relatively high-risk levels, while systolic and diastolic blood pressure risks were extremely low, suggesting that the impairment was mainly confined to the metabolic system. Class 3: Cardiovascular-metabolic high-load group (19.4%, n = 165). Pregnant women in this group showed high risks in both cardiovascular and metabolic indicators, with systolic blood pressure, diastolic blood pressure, fasting blood glucose, and total cholesterol at relatively high levels, and high-sensitivity C-reactive protein at a moderately elevated level, representing a multisystem combined impairment group. Class 4: Multisystem combined high-load group (60.5%, n = 514). Pregnant women in this group had the

highest high-risk probabilities across all eight indicators, reflecting significant physiological dysregulation across multiple systems, representing the subgroup with the most severe chronic stress accumulation. The conditional probability plot of the AL latent classes is shown in Figure 1.

2.3 Univariate analysis of influencing factors for latent classes of allostatic load among women

The results of the univariate analysis are presented in Table 3. Gestational week ($\chi^2 = 26.249, P < 0.001$), adverse pregnancy history ($\chi^2 = 10.528, P = 0.015$), and anxiety ($\chi^2 = 33.493, P < 0.001$) showed statistically significant differences across the four latent classes of AL. Age ($\chi^2 = 1.380, P = 0.710$), education level ($\chi^2 = 2.837, P = 0.417$), occupation ($\chi^2 = 21.384, P = 0.125$), history of alcohol consumption ($\chi^2 = 0.957, P = 0.812$), depression ($\chi^2 = 5.546, P = 0.136$), physical activity level ($\chi^2 = 3.058, P = 0.802$), and pregnancy complications ($\chi^2 = 5.236, P = 0.155$) showed no statistically significant differences among the classes. Specifically, the multisystem combined high-load group had the highest proportion of pregnant women in the third trimester (73.8%), and this group also had the highest proportion of pregnant women with anxiety (67.8%).

Table 3 Univariate Analysis of Influencing Factors for Latent Classes of Allostatic Load Among Women[n%]

Variable	Category	Low-load group n=99	Metabolic high-load group (n = 72)	Cardiovascular-metabolic high-load group (n = 165)	Multisystem combined high-load group (n = 514)	Statistic	P-value
Age	<35	19.1	0.0	327.3	763.6	$\chi^2=1.380$	0.710
	≥35	98 11.7	728.6	16219.3	50760.4		
Gestational week	Second trimester	115.2	199.0	2511.9	15573.8	$\chi^2=26.249$	<0.001
	Third trimester	88 13.8	538.3	14021.0	35956.1		
Education level	Bachelor's degree or below	71 11.7	569.2	12320.2	35958.9	$\chi^2=2.837$	0.417
	Bachelor's degree or above	28 11.6	166.6	4217.4	15564.3		
Occupation	Unemployed	16 19.0	56.0	1922.6	4452.4	$\chi^2=21.384$	0.125
	Administrative staff	169.4	127.0	4425.7	9957.9		
	Head of unit	16.7	16.7	426.7	960.0		
	Commercial service personnel	710.3	22.9	1522.1	4464.7		
	Professional and technical personnel	23 14.0	148.5	2716.5	10061.0		
	Other	36 10.3	3810.9	5619.4	21862.6		
Adverse pregnancy history	Yes	12 12.6	88.4	2829.5	4749.5	$\chi^2=10.528$	0.015
	No	488.8	509.2	9417.3	35164.6		
Alcohol drinking history	Yes	316.7	211.1	422.2	950.0	$\chi^2=0.957$	0.812
	No	96 11.5	708.4	16119.4	50660.7		
Anxiety	Yes	448.5	438.3	7915.3	34967.8	$\chi^2=33.493$	<0.001
	No	55 16.4	298.7	8625.7	16549.3		
Depression	Yes	410.8	718.9	718.9	1951.4	$\chi^2=5.546$	0.136
	No	95 11.7	658.0	15819.4	49560.9		
Physical activity level	Low	25 11.9	2110.0	4019.0	12459.0	$\chi^2=3.058$	0.802
	Moderate	59 12.4	357.4	9419.8	28660.3		
	High	159.0	169.6	3118.7	10462.7		
Pregnancy complications	Yes	62 13.8	388.5	9020.0	25957.7	$\chi^2=5.236$	0.155
	No	379.2	348.5	7518.7	25563.6		

2.4 Multivariate analysis of influencing factors for latent classes of allostatic load among women

Variables with $P < 0.1$ in the univariate analysis (i.e., gestational week, adverse pregnancy history, and anxiety) were entered as independent variables into a multinomial logistic regression model, with the four latent classes of AL as the dependent variable and Class 4 (the multisystem combined high-load group) set as the reference category. Multivariate analysis revealed that anxiety was an independent influencing factor for AL latent class membership. Compared with pregnant women with anxiety, those without anxiety had significantly higher odds of being classified into Class 1 (low-load group; OR = 2.243, 95% CI: 1.081–4.653, $P = 0.030$), Class 2 (metabolic high-load group; OR = 2.570, 95% CI: 1.199–5.508, $P = 0.015$), and Class 3 (cardiovascular-metabolic high-load group; OR = 2.428, 95% CI: 1.358–4.342, $P = 0.003$). This finding indicates that pregnant women with anxiety were more likely to be classified into the multisystem combined high-load group. Gestational week and adverse pregnancy history were not retained in the final multivariate model (all $P > 0.05$). Variable assignments are presented in Table 4, and the results of the multinomial logistic regression analysis are presented in Table 5.

Table 4 Variable Assignment for Multinomial Logistic Regression

Variable	Assignment
Age	$<35 \geq 35 = 2$
Gestational week	First trimester = 1 Second trimester = 2 Third trimester = 3
Education level	Bachelor's degree or below = 1, Bachelor's degree or above = 2
Occupation	Unemployed = 0, Administrative staff = 1, Head of unit = 2, Commercial service personnel = 3, Professional and technical personnel = 4, Other = 5
Adverse pregnancy history	No = 0, Yes = 1
Alcohol drinking history	No = 0, Yes = 1
Anxiety	No = 0, Yes = 1
Depression	No = 0, Yes = 1
Physical activity level	Low = 0, Moderate = 1, High = 2
Pregnancy complications	No = 0, Yes = 1

Table 5 Multinomial Logistic Regression Analysis of Factors Associated With Latent Classes of Allostatic Load Among Pregnant Women

Class	Variable	Category	OR	95% CL	P-value
Class 1: Low-load group	Gestational week	Second trimester	0.565	[0.259–1.233]	0.152
	Adverse pregnancy history	No	1.043	[0.484–2.248]	0.914
	Anxiety	No	2.243	[1.081–4.653]	0.030
Class 2: Metabolic high-load group	Gestational week	Second trimester	1.072	[0.533–2.155]	0.846
	Adverse pregnancy history	No	1.177	[0.483–2.871]	0.720
	Anxiety	No	2.570	[1.199–5.508]	0.015
Class 3: Cardiovascular-metabolic high-load group	Gestational week	Second trimester	0.643	[0.369–1.121]	0.120
	Adverse pregnancy history	No	0.716	[0.399–1.287]	0.264
	Anxiety	No	2.428	[1.358–4.342]	0.003

Note: This table uses Class 4 (multisystem combined high-load group) among the four latent classes as the reference. The reference categories for variables were ≥ 35 years, third trimester, bachelor's degree or above, other occupations, having adverse pregnancy history, having alcohol drinking history, having anxiety, having depression, high physical activity level, and having pregnancy complications.

3 Discussion

3.1 There are four clinically distinguishable physiological subtypes of allostatic load during pregnancy

Using latent class analysis (LCA), we analyzed eight multisystem biomarkers among 850 pregnant women in the second and third trimesters, and identified four distinct AL subtypes characterized by heterogeneous patterns of physiological dysregulation: the low-load group, the metabolic high-load group, the cardiometabolic high-load group, and the multisystem combined high-load group. Our findings address key limitations of the conventional dichotomous classification approach based on aggregate AL scores^[13]. Compared with the three AL subtypes (the low-dysregulation group, the metabolic-immune dysregulation group, and the cardiovascular dysregulation group) identified by Zhou et al.^[5] among 637 Chinese women recruited solely during the second trimester, our study further refined AL classification by including both second- and third-trimester participants. The large proportion of multisystem combined high-load women in our sample may be partly explained by physiological remodeling in late-gestation. Additionally, our study extended prior work by examining psychological correlates of AL latent classes. Specifically, we not only distinguished cardiovascular dysregulation from metabolic-immune dysregulation, but also identified the multisystem combined high-load group as the most prevalent subtype, accounting for 60.5% of the cohort. This discrepancy likely stems from differences in gestational stages across the study populations. In our cohort, 75.3% of participants were in the third trimester, a period during which maternal blood volume increases by approximately 40%~50% and cardiac output rises significantly^[25]. Meanwhile, physiological insulin resistance is exacerbated by elevated levels of insulin-antagonistic hormones secreted by the placenta, such as human placental lactogen and cortisol^[26]. Together, these adaptive changes render women in the third trimester more susceptible to combined multisystem impairment. The predominance of Class 4 (the multisystem combined high-load group), which accounted for 60.5% of participants, supports this inference, indicating that combined multisystem impairment is the dominant AL profile in the third trimester.

The metabolic high-load group was primarily characterized by metabolic abnormalities, with high item-response probabilities for waist circumference (0.73), BMI (0.91), high-sensitivity C-reactive protein (0.76), and fasting blood glucose (0.81), and extremely low probabilities for systolic blood pressure (0.00) and diastolic blood pressure (0.10). This pattern suggests that physiological impairment in this group was largely restricted to the metabolic system. The underlying mechanism may involve gestational weight gain and physiological elevations in blood lipids, which, when combined with a high-sugar, high-fat dietary pattern and sedentary behavior, readily lead to cumulative impairment of glucolipid metabolism^[27]. This finding is consistent with the study by Barry et al.^[16] conducted in metabolically abnormal preconception women. The cardiovascular-metabolic high-load group exhibited high response probabilities

across both cardiovascular and metabolic indicators. Specifically, systolic blood pressure (0.90), diastolic blood pressure (0.71), waist circumference (0.80), BMI (0.91), and fasting blood glucose (0.81) all showed relatively high probabilities, while high-sensitivity C-reactive protein (0.74) was moderately elevated, presenting features of combined multisystem impairment. Obesity and dysglycemia during pregnancy can stimulate adipose tissue to secrete pro-inflammatory cytokines, including interleukin-6 and tumor necrosis factor- α . In turn, inflammatory signals further exacerbate metabolic disturbances by disrupting insulin signaling pathways^[10], creating a vicious metabolic-inflammatory cycle that markedly increases the risk of preterm premature rupture of membranes and pregnancy-related infectious complications^[5]. Accordingly, this subgroup should be recognized as a priority population for obstetric monitoring.

3.2 Anxiety is a core influencing factor differentiating AL subtypes

Multinomial logistic regression analysis revealed that anxiety was the only independent influencing factor retained in the final model. Compared with pregnant women with anxiety, those without anxiety had significantly higher odds of being classified into the low-load group (OR = 2.243, 95% CI: 1.081–4.653, $P=0.030$), the metabolic high-load group (OR = 2.570, 95% CI: 1.199–5.508, $P = 0.015$), and the cardiovascular-metabolic high-load group (OR = 2.428, 95% CI: 1.358–4.342, $P = 0.003$), indicating that pregnant women with anxiety were more likely to be assigned to the multisystem combined high-load group. This finding aligns with those of previous studies. Wang et al.^[6] reported a significant association between early-pregnancy allostatic load and depression (OR = 1.651), and Yuan et al.^[13] further demonstrated that depressive symptoms were associated with a 6.24-fold increase in the odds of high AL (OR = 6.241). Our study extends this line of evidence from depression to anxiety, and provides the first confirmation of the independent effect of anxiety on AL latent class membership within a multicategorical framework. The underlying mechanism involves pregnancy-related anxiety activating the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic–adrenal–medullary system, leading to the sustained release of glucocorticoids and catecholamines, which in turn drives elevated blood pressure, dysglycemia, and immune-inflammatory responses^[28]. Chronic anxiety may also indirectly exacerbate metabolic disturbances by altering lifestyle behaviors^[14]. These findings indicate that pregnancy-related anxiety is not merely a psychological concern, but also a critical upstream driver of multisystem physiological wear and tear.

Notably, gestational week was statistically significant in the univariate analysis ($P<0.001$), but this significance was attenuated to non-significance after adjusting for anxiety in the multivariate model. This pattern suggests that the association between gestational week and AL class membership may be partially mediated by anxiety. As gestation progresses, increased physical burden, sleep deprivation, and pronounced fluctuations in pregnancy-related hormone levels may exacerbate anxiety symptoms, thereby driving elevations in AL^[11]. This finding highlights early pregnancy as a critical window for mental health screening; early identification of anxiety may help interrupt the pathway leading to physiological wear and tear^[23,28]. Alcohol consumption showed no statistically significant association with AL latent classes in the univariate analysis, a finding inconsistent with prior evidence^[29]. This discrepancy may be attributable to the relatively low prevalence of alcohol drinking history among pregnant women in our cohort. Future studies may further investigate the dose–response relationship between alcohol consumption and AL during pregnancy.

3.3 Implications for primary and community maternal health care

Our findings have clear translational value for primary and community maternal health care practice. Anxiety should be considered a core screening and intervention target throughout pregnancy. It is recommended that a three-tiered pathway of “psychological screening – physiological phenotyping – stratified intervention”^[30] be embedded within the existing maternal health management framework: ☐ At the first antenatal visit (early pregnancy), use the Pregnancy-Related Anxiety Questionnaire for anxiety screening. Those who screen positive should receive brief psychological interventions based on mindfulness or cognitive-behavioral therapy provided by community nurses or mental health professionals^[28]; ☐ Based on three core indicators routinely measured during antenatal check-ups—blood pressure, waist circumference, and fasting blood glucose—combined with gestational week information, perform preliminary phenotyping according to the four-class criteria from this study: those with abnormal blood pressure should be prioritized for cardiovascular-metabolic combined impairment; those with isolated waist circumference/blood glucose abnormalities should be prioritized for metabolic interventions; those with all indicators within normal ranges should receive routine management; ☐ For pregnant women with existing metabolic or cardiovascular system abnormalities, psychological status should be addressed concurrently with dietary and exercise prescriptions to avoid anxiety exacerbating physiological wear and tear through HPA axis activation^[21].

4 Strengths and Limitations

This study offers several notable strengths, including the use of cross-sectional surveys at both the second and third trimesters, which provides a comprehensive characterization of maternal allostatic load profiles across mid-to-late pregnancy and overcomes the

limitations of single-time-point assessments. Unlike prior work focused solely on physiological measures, we integrated objective biomarkers with psychological scales, allowing us to identify anxiety- and depression-related factors associated with latent class membership, and the application of latent class analysis enabled objective categorization of heterogeneous subgroups, supporting stratified antenatal care. However, several limitations should be acknowledged. The recruitment of all participants from tertiary hospitals in a single province may limit generalizability, and key stress-related variables such as social support, pregnancy-specific stress, and adverse pregnancy experiences were not assessed. Furthermore, as an observational study, causal inferences cannot be drawn, and the inclusion of only one immune marker (hs-CRP) without neuroendocrine indicators like cortisol may restrict our ability to detect immune- or neuroendocrine-dominant subtypes, potentially influencing latent class classification and interpretation. More comprehensive panels of allostatic-load biomarkers are recommended for future investigations.

5 Conclusion

Pregnant women exhibit significant heterogeneity in allostatic load (AL), which can be divided into four subtypes with distinct physiological dysregulation characteristics: Low Load Group (11.6%), Metabolic High Load Group (8.5%), Cardiovascular-Metabolic High Load Group (19.4%) and Multi-system Combined High Load Group (60.5%). Anxiety is a key independent factor differentiating these subtypes, and pregnant women with anxiety are more likely to fall into the Multi-system Combined High Load Group. It is recommended that anxiety screening be included in routine antenatal examinations at community health service centers and obstetric clinics, and targeted stratified interventions be implemented according to the physiological features of each subtype to reduce the health risks of chronic stress for mothers and their offspring.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Anhui Medical University (Approval No. s20210076) and the original cohort study was registered in the Chinese Clinical Trial Registry (ChiCTR2200066044). All participants provided written informed consent prior to enrollment.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest

All authors declare that there is no conflict of interest.

Funding Declaration

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Authors' contributions

Guangxiu Zhao: Data curation, Formal analysis, Writing – original draft.

Yuan Xu: Data curation, Writing – original draft.

Yuhong Li: Conceptualization, Supervision, Quality control, Writing – review & editing, overall responsibility for this manuscript.

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Figures

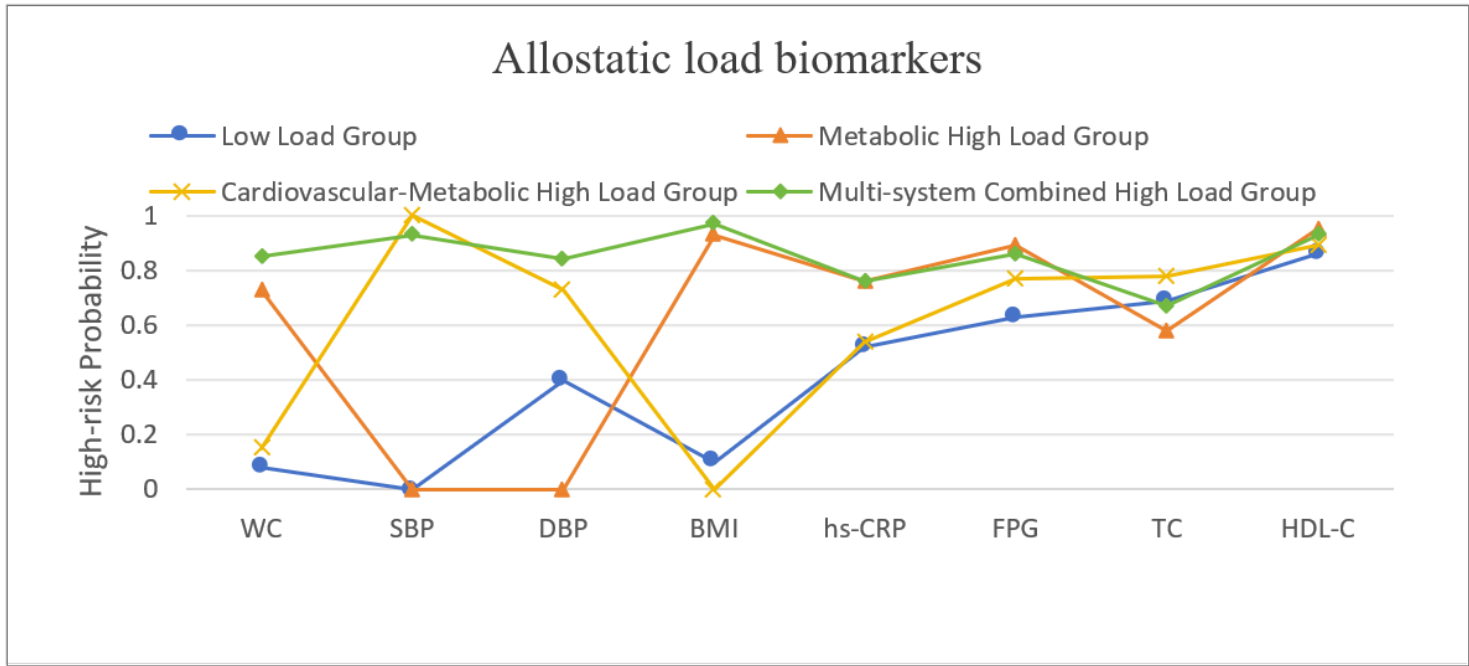


Figure 1

Latent Class Profile Plot of Allostatic Load Among Pregnant Women