

## Postprint: Correlation Between Dietary Inflammatory Index and Delayed Onset of Lactation in Third-Trimester Pregnant Women

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**Date:** 2025-04-07T00:00:00+00:00

### Abstract

**Background** Delayed onset of lactation (DOL) is an important cause of reduced exclusive breastfeeding rates. The Dietary Inflammatory Index (DII) has been confirmed to be associated with various adverse health outcomes, but its relationship with DOL is not yet well understood.

**Objective** To investigate DII levels in third-trimester pregnant women and explore its impact on DOL.

**Methods** Using convenience sampling, third-trimester women undergoing routine prenatal care at the First Affiliated Hospital of Anhui Medical University from December 2023 to June 2024 were selected as study subjects and followed up until 72 hours postpartum. DOL status was determined using the maternal self-perceived breast fullness method. A general information questionnaire was used to collect demographic characteristics and pregnancy-related information; a Food Frequency Questionnaire (FFQ) was used to collect dietary intake information and calculate DII; a delivery and postpartum information questionnaire was used to collect delivery and postpartum-related information. Binary logistic regression analysis was used to explore the relationship between DII and DOL, with stratified analysis conducted for age, pre-pregnancy BMI, and gestational diabetes mellitus status.

**Results** A total of 228 questionnaires were distributed, with 217 valid questionnaires recovered (effective recovery rate: 95.2%). Among these, 68 women (31.3%) developed DOL. Statistically significant differences between DOL and non-DOL mothers were found in gravidity, sleep quality during pregnancy, gestational weight gain, and mother-infant separation postpartum ( $P < 0.05$ ). Based on tertiles, DII was divided into low, medium, and high groups. The high DII group had a higher DOL incidence than the medium and low DII groups ( $P < 0.05$ ). Binary logistic regression analysis showed that the risk of DOL in

the high DII group was 2.817 times that of the low DII group (95% CI = 1.244–6.381,  $P=0.013$ ). In subgroups of third-trimester women with age <35 years and pre-pregnancy BMI <24.0 kg/m<sup>2</sup>, women with high DII levels had DOL risks of 3.144 times (95% CI = 1.346–7.344,  $P<0.05$ ) and 2.666 times (95% CI = 1.072–6.630,  $P<0.05$ ) compared to those with low DII levels, respectively.

**Conclusion** There is a correlation between DII and DOL, with higher DII increasing DOL risk, particularly in third-trimester women with age <35 years and pre-pregnancy BMI <24.0 kg/m<sup>2</sup>. Maternal and child health care providers should offer personalized dietary guidance to pregnant women, increasing anti-inflammatory dietary intake to reduce DOL incidence and improve exclusive breastfeeding rates.

## Full Text

### Correlation between Dietary Inflammatory Index and Delayed Onset of Lactogenesis in Late Pregnancy

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## Abstract

**Background:** Delayed onset of lactogenesis (DOL) is a significant factor contributing to reduced exclusive breastfeeding rates. While the dietary inflammatory index (DII) has been associated with various adverse health outcomes, its relationship with DOL remains unclear. **Objective:** To investigate DII levels among women in the third trimester and examine their impact on DOL. **Methods:** Using convenience sampling, we recruited third-trimester women receiving routine prenatal care at The First Affiliated Hospital of Anhui Medical University from December 2023 to June 2024, following them until 72 hours postpartum. DOL status was determined using maternal self-perceived breast distension. General demographic and pregnancy-related information was collected via a general information questionnaire. Dietary intake was assessed using a food frequency questionnaire (FFQ) to calculate DII scores. Delivery and postpartum information was gathered through a dedicated survey. Binary logistic regression analysis was employed to explore the relationship between DII and DOL, with stratification by age, pre-pregnancy BMI, and gestational diabetes mellitus status. **Results:** Of 228 distributed questionnaires, 217 were validly returned (95.2% response rate). DOL occurred in 68 women (31.3%). Significant differences between DOL and non-DOL groups were observed in gravidity, sleep quality during pregnancy, gestational weight gain, and mother-

infant separation postpartum ( $P < 0.05$ ). Using tertiles, DII was categorized into low, medium, and high groups. The high DII group exhibited a higher DOL incidence than the medium and low groups ( $P < 0.05$ ). Binary logistic regression revealed that the high DII group had 2.817 times higher risk of DOL compared to the low DII group (95%CI=1.244-6.381,  $P = 0.013$ ). Among women aged  $< 35$  years and with pre-pregnancy BMI  $< 24.0$  kg/m<sup>2</sup>, those with high DII levels showed 3.144 times (95%CI=1.346-7.344,  $P < 0.05$ ) and 2.666 times (95%CI=1.072-6.630,  $P < 0.05$ ) higher DOL risk, respectively, compared to low DII levels. **Conclusion:** DII correlates with DOL, with higher DII increasing DOL risk, particularly among third-trimester women aged  $< 35$  years and with pre-pregnancy BMI  $< 24.0$  kg/m<sup>2</sup>. Maternal and child healthcare providers should offer personalized dietary guidance to pregnant women, promoting anti-inflammatory diets to reduce DOL incidence and improve exclusive breastfeeding rates.

**Keywords:** Lactation; Delayed onset of lactogenesis; Dietary inflammatory index; Inflammatory factors; Pro-inflammatory diet; Correlation analysis

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## Introduction

The *Chinese Dietary Guidelines (2022)* emphasize that breast milk is the optimal food for infants, recommending exclusive breastfeeding for the first six months. However, surveys indicate that exclusive breastfeeding rates in China and globally fall far short of the 50% target set by the World Health Assembly[1]. Research demonstrates that delayed onset of lactogenesis (DOL) is a major contributor to low exclusive breastfeeding rates[2]. DOL, or delayed stage II lactogenesis, is defined as the absence of noticeable breast fullness or distension within 72 hours postpartum[3]. Reportedly, DOL affects up to 31.5% of women in China[4], compromising not only breastfeeding success but also increasing risks of neonatal pathological weight loss and infectious diseases, thereby seriously impacting maternal and infant health[5].

Existing studies suggest associations between inflammatory markers—such as interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and C-reactive protein (CRP)—and lactation, though findings remain inconsistent[6-7]. Diet significantly modulates these inflammatory markers. The dietary inflammatory index (DII), a novel method for assessing dietary quality and inflammatory potential, quantifies the inflammatory impact of diet on the body[8]. DII has been linked to obesity[9], cardiovascular disease and cancer[10], and adverse pregnancy outcomes[11], yet research on its relationship with DOL is limited. The third trimester represents a critical period for maternal and infant health and an ideal window for intervention[12]. Therefore, this study examines DII levels in late pregnancy and explores its effects on DOL, aiming to improve postpartum lactation outcomes and help achieve the *China Child Development Outline (2021-2030)* goal of exceeding 50% exclusive breastfeeding rate among 0-6

month infants[13].

## Methods

**1.1 Study Participants** Using convenience sampling, we recruited pregnant women attending prenatal examinations at The First Affiliated Hospital of Anhui Medical University from December 2023 to June 2024, following them until 72 hours postpartum. Sample size calculation using PASS software determined a requirement of 135 participants; accounting for 20% attrition, the target sample was 169.

**Inclusion criteria:** (1) Singleton pregnancy  $\geq 32$  weeks gestation; (2) Good breast development with intention to breastfeed; (3) Ability to complete surveys accurately with researcher guidance; (4) Voluntary informed consent.

**Exclusion criteria:** (1) Breastfeeding contraindications; (2) Psychiatric disorders or intellectual disability; (3) Severe physical illness or drug abuse history; (4) Abnormal diet in the preceding month.

**Exclusion during follow-up:** (1) Women who discontinued breastfeeding postpartum for any reason; (2) Incomplete data or loss to follow-up.

This study was approved by the Biomedical Ethics Committee of Anhui Medical University (Approval No.: 83242343).

## 1.2 Survey Instruments and Procedures 1.2.1 General Information

**Questionnaire:** Collected demographic and pregnancy-related data including age, occupation[14], education level, residence, household income per capita, pre-pregnancy BMI, gravidity and parity, history of breast surgery or nipple abnormalities, exposure to stressful life events in early pregnancy, sleep quality, gestational diabetes mellitus, gestational hypertension, and physical activity (PA).

Pre-pregnancy BMI was evaluated using the *Chinese Women's Gestational Weight Monitoring and Evaluation* standards issued by the Chinese Nutrition Society in 2021:  $<18.5 \text{ kg/m}^2$  (underweight),  $18.5\text{--}23.9 \text{ kg/m}^2$  (normal weight),  $24.0\text{--}27.9 \text{ kg/m}^2$  (overweight), and  $\geq 28.0 \text{ kg/m}^2$  (obese)[15]. Sleep quality was self-rated as poor, fair, or good[4]. PA was assessed using the International Physical Activity Questionnaire-Short Form (IPAQ-SF), a validated instrument with good reliability and validity[16]. Weekly energy expenditure for each intensity level was calculated as: MET value  $\times$  frequency (days/week)  $\times$  duration (minutes/day). MET values for high, moderate, and low intensity PA were 8.0, 4.0, and 3.3, respectively[17]. High-intensity PA included activities requiring substantial effort with markedly increased breathing (e.g., heavy lifting, running, swimming). Moderate-intensity PA involved some effort with slightly increased breathing (e.g., light lifting, mopping, window cleaning, excluding walking). Low-intensity PA included work, household, transportation,

and walking for exercise[18]. PA levels were categorized as high, moderate, or low based on specific criteria .

**1.2.1.2 Food Frequency Questionnaire (FFQ):** A semi-quantitative FFQ combined with the *Retrospective Dietary Survey Auxiliary Reference Food Atlas* was used to collect dietary intake frequency and average portion sizes over the preceding month. The FFQ, designed based on Chinese dietary habits and validated for pregnant women, demonstrated good reliability (correlation coefficients: 0.23–0.49 for food groups, 0.24–0.58 for nutrients) and validity (correlation coefficients: 0.35–0.56 for food groups, 0.11–0.63 for nutrients)[19]. Trained professionals conducted face-to-face interviews using the Food Atlas to enhance accuracy.

**1.2.1.3 Delivery and Postpartum Information Questionnaire:** Collected data via face-to-face interviews, medical record review, and telephone follow-up on gestational weight gain, infant birth weight, delivery mode, labor duration, breastfeeding initiation, and lactogenesis onset time.

Gestational weight gain was evaluated according to the 2021 Chinese Nutrition Society standards: total weight gain ranges of 11.0–16.0 kg, 8.0–14.0 kg, 7.0–11.0 kg, and 5.0–9.0 kg for underweight, normal weight, overweight, and obese pre-pregnancy BMI categories, respectively. Weight gain within the recommended range was considered appropriate; below or above was classified as insufficient or excessive[15]. Infant birth weight categories were <2,500 g, 2,500–3,600 g, and >3,600 g.

**1.2.2 DOL Assessment:** Lactogenesis onset was determined using maternal self-perceived breast distension[22]. Trained investigators inquired daily about breast sensations: (1) no fullness or distension; (2) slight fullness; (3) obvious or uncomfortable fullness/distension. Women reporting (1) or (2) were followed until 72 hours postpartum; persistent reports of (1) or (2) at 72 hours defined DOL, while report of (3) indicated non-DOL status.

**1.2.3 DII Calculation:** (1) Dietary data were collected via FFQ. (2) Using the *China Food Composition Table*, nutrient contents were converted to match DII components and compared against global standard dietary intake databases to calculate Z-scores:  $Z = (\text{daily intake} - \text{global mean daily intake}) / \text{global standard deviation}$ . (3) Z-scores were converted to percentiles, doubled and subtracted by 1 to create a symmetric distribution centered at zero, then multiplied by the inflammatory effect score for each component. (4) Component scores were summed to obtain the total DII score, where higher scores indicate greater pro-inflammatory potential and lower scores indicate anti-inflammatory potential.

**1.2.4 Quality Control:** Investigators received unified training to strictly apply inclusion/exclusion criteria and obtain informed consent. Face-to-face interviews ensured accuracy, with food conversion tables provided for FFQ completion. Questionnaires were reviewed immediately upon collection.

**1.3 Statistical Analysis** Data were entered and verified using Excel, with statistical analysis performed in SPSS 23.0. Categorical data were expressed as frequencies and percentages, compared using  $\chi^2$  tests or Fisher's exact test. Non-normally distributed continuous data were presented as median (P25, P75) and compared using non-parametric tests. Variables significant in univariate analysis were included as covariates. Binary logistic regression examined the relationship between DII and DOL, with stratified analyses conducted. Statistical significance was set at  $P < 0.05$ .

## Results

**2.1 Participant Characteristics** Of 228 distributed questionnaires, 217 were validly returned (95.2% response rate) after excluding 6 women who discontinued breastfeeding and 5 lost to follow-up. DOL occurred in 68 women (31.3%). Significant differences between DOL and non-DOL groups were found in gravidity, sleep quality during pregnancy, gestational weight gain, and mother-infant separation postpartum ( $P < 0.05$ ). No significant differences were observed in age, occupation, education, residence, household income, or pre-pregnancy BMI.

**2.2 DII Distribution and DOL Incidence** DII scores ranged from -3.75 to 4.06, with a median of 1.01 (-0.16, 2.12). Using tertiles[23], participants were divided into low ( $n=72$ ; DII: -3.75 to  $<0.24$ ), medium ( $n=73$ ; DII: 0.24-1.75), and high ( $n=72$ ; DII:  $>1.75$ -4.06) DII groups. DOL incidence differed significantly across groups ( $\chi^2=10.768$ ,  $P=0.005$ ), with the high DII group showing higher incidence than medium and low groups ( $P < 0.05$ ).

**2.3 Impact of DII on DOL** Binary logistic regression with DOL as the dependent variable (0=no, 1=yes) and DII group as the independent variable (0=low, 1=medium, 2=high) showed high DII as a risk factor for DOL in the unadjusted model (Model 1,  $P < 0.05$ ).

After adjusting for significant univariate variables (gravidity, sleep quality, gestational weight gain, mother-infant separation) and additional covariates based on literature (age, pre-pregnancy BMI, gestational diabetes, gestational hypertension, total energy intake) to enhance robustness (Model 2), high DII remained associated with 2.817 times higher DOL risk compared to low DII (95%CI=1.244-6.381,  $P=0.013$ ).

**2.4 Stratified Analysis** Stratified logistic regression examined whether the DII-DOL relationship varied by age ( $<35$  vs.  $\geq 35$  years), pre-pregnancy BMI ( $<24.0$  vs.  $\geq 24.0 \text{ kg/m}^2$ ), and gestational diabetes status[24].

Model 1 (unadjusted) showed that among women aged  $<35$  years, with pre-pregnancy BMI  $<24.0 \text{ kg/m}^2$ , and without gestational diabetes, high DII was associated with increased DOL risk ( $P < 0.05$ ). After adjusting for gravidity,

sleep quality, gestational weight gain, and mother-infant separation (Model 2), high DII remained a significant risk factor among women aged <35 years (OR=3.144, 95%CI=1.346-7.344) and those with pre-pregnancy BMI<24.0 kg/m<sup>2</sup> (OR=2.666, 95%CI=1.072-6.630) (both P<0.05). No significant interactions were found for gestational diabetes .

## Discussion

**3.1 DOL Incidence and DII Status** The 31.3% DOL incidence aligns with Ding et al.'s report of 31.5%[4] but is lower than Lu et al.'s 36.36%[25], likely due to different sample characteristics. Given DOL' s high prevalence and adverse consequences for maternal and infant health[24], healthcare providers should prioritize high-risk groups to reduce DOL incidence and achieve national exclusive breastfeeding targets.

Our findings reveal elevated DII scores among third-trimester women, consistent with Lin et al.[26] and Qin et al.[11], indicating a pro-inflammatory dietary pattern characterized by high intake of refined carbohydrates, saturated fats, and energy-dense foods. This may stem from traditional beliefs promoting high-nutrient foods during pregnancy. However, elevated DII is associated with adverse outcomes including increased gestational diabetes risk[27] and higher rates of fetal distress and low birth weight[11], underscoring the need for balanced, anti-inflammatory dietary patterns.

**3.2 Correlation Between DII and DOL** Maternal nutrition fundamentally supports lactation; adequate, balanced diets improve milk quality, composition, and help restore maternal nutrient reserves and organ function[28-29]. Conversely, excessive high-fat diets (pro-inflammatory[30]) impair mammary lobular development and differentiation, reducing milk production[31]. Our results confirm a positive DII-DOL association, with high DII conferring 2.817 times greater DOL risk. DII reflects inflammatory biomarker levels (CRP, TNF- $\alpha$ , IL-1 $\beta$ , IL-4, IL-6, IL-10)[32]. Pro-inflammatory cytokines IL-6 and TNF- $\alpha$  regulate mammary development and function, influencing milk secretion[33]; reduced levels increase serum prolactin and promote earlier lactogenesis[6]. Pregnancy induces a dynamic, regulated inflammatory response[34], and pro-inflammatory diets may exacerbate chronic inflammation, elevate inflammatory markers, reduce prolactin, and increase DOL risk.

Stratified analysis revealed stronger DII effects among women aged <35 years and with pre-pregnancy BMI<24.0 kg/m<sup>2</sup>. Zhang[35] similarly found stronger associations between pro-inflammatory diets and gestational diabetes risk in younger women (<30 years). Pro-inflammatory diets may cause insulin resistance through chronic inflammation[34]; insulin resistance with overexpressed protein tyrosine phosphatase receptor type F reduces insulin activity, slowing milk production[36]. International research suggests normal-weight individuals may experience greater inflammatory responses to pro-inflammatory diets

than obese individuals, possibly because obese individuals may adopt anti-inflammatory diets to alleviate discomfort[37].

### Limitations

This study's limitations include: (1) single-hospital sample limiting generalizability; (2) potential subjective and recall bias inherent to FFQ; (3) assessment limited to third-trimester diet. Future research should examine dietary patterns across pregnancy stages to clarify the DII-DOL association and provide broader theoretical support for clinical interventions.

### Author Contributions

CHEN Huiyu: conceptualization, data analysis, manuscript writing and revision. XU Ziyang: data processing and cleaning. LI Yuhong: supervision of study design, quality control, and manuscript review, with overall responsibility. All authors approved the final manuscript.

**Conflict of Interest:** None declared.

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*Received: 2025-01-12; Revised: 2025-03-20*

*Edited by: JIA Mengmeng*

*Note: Figure translations are in progress. See original paper for figures.*

*Source: ChinaXiv – Machine translation. Verify with original.*