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The influence of dietary choices: investigation of the relationship dietary inflammatory index and fetal growth restriction

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Abstract

Background Fetal growth restriction (FGR) is characterized by the fetus's inability to reach its growth potential and affecting approximately 10% of the population. The etiology of late-onset FGR, which occurs after 32 weeks, is unclear but may be influenced by maternal weight. A proinflammatory diet can cause chronic inflammation and, Dietary Inflammatory Index (DII) was developed to evaluate of the diet's impact on inflammation. A high DII indicates a pro-inflammatory diet, known to increase serum inflammatory markers, with oxidative stress playing a key role in inflammatory diseases. The study aimed to investigate the correlation between maternal DII, total oxidant status (TOS), total antioxidant status (TAS), interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF-α) levels in FGR-diagnosed pregnant women.

Methods This prospective-observational study included FGR-diagnosed pregnant women and healthy pregnant women with gestational ages of 32–38 weeks ($n=23$ per group). Chronic diseases, hypertension, fetal anomalies, membrane ruptures, and multiple pregnancies were excluded. The DII was calculated using the BeBiS-9 program based on 3-day dietary records kept by an expert dietician. Blood samples were collected, centrifuged, and analyzed for IL-6, TNF-α, IL-10, TAS, and TOS.

Results The study group had significantly higher DII scores ($p<0.001$), lower energy ($p=0.004$), carbohydrate ($p=0.002$), protein ($p=0.011$), fiber ($p<0.001$) intake than the control group. TNF-α levels were elevated in the FGR group ($p<0.001$), while IL-6 levels were higher but not statistically significant ($p=0.06$). IL-10 levels were lower in the study group ($p=0.05$). TAS, TOS, and TAS/TOS levels showed no significant differences between groups. Logistic regression indicated a 62% increase in FGR probability with higher DII levels ($p=0.001$, CI 1.209–2.195). Correlation analysis revealed a strong positive correlation between DII and maternal serum TNF-α ($r=0.375$, $p=0.01$) and a strong negative correlation between birth weight and TNF-α (r=-0.478, $p<0.001$) and DII (r=-0.446, $p=0.002$).

Conclusion This study showed that a pro-inflammatory maternal diet increased dietary inflammatory index and increased maternal inflammatory markers, and this was more significant in fetuses with FGR than in normal weight fetuses.

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Keywords Fetal growth restriction, Dietary inflammatory index, IL-6, IL-10, TNF-α, Total antioxidant status, Total oxidant status

Introduction

Good maternal nutritional and metabolic status is essential for maintaining a healthy pregnancy. It is known that many chronic adult diseases are associated with the fetal period. The placenta is the major organ that is constantly growing and providing feto-maternal transport for the needs of the fetus. This transport can be directly influenced by the concentration of essential nutrients in maternal plasma, which are important for fetal development. Therefore, an adequate and balanced diet during pregnancy is very important [1].

Fetal growth restriction (FGR) denotes the fetus's failure to attain its growth potential due to several factors, including genetic, infectious, and placental anomalies. FGR affects 10% of the general population and is a significant contributor to perinatal morbidity and mortality [2]. Fetal growth restriction (FGR) is often diagnosed when the estimated fetal weight or abdominal circumference (AC) falls below the 10th percentile for the corrected gestational age [3, 4]. The Delphi agreement states that a fetal AC or estimated fetal weight (EFW) below the 10th percentile, accompanied by Doppler abnormalities, or either AC or EFW below the 3rd percentile without Doppler findings, validates the diagnosis of FGR [5]. The classification of FGR is contingent upon the timing of onset; early-onset FGR is defined by the emergence of symptoms prior to 32 weeks of gestation, whereas late-onset FGR is defined by the emergence of symptoms subsequent to 32 weeks of gestation [6]. Early onset FGR is observed in 1% of the population and is predominantly associated with pathological processes including pre-eclampsia, genetic disorders and TORCH infections. In contrast, late-onset FGR is more prevalent, from 5% up to 10% [2]. The reason of late-onset FGR is still uncertain, although studies have shown a relationship with maternal weight [7].

A proinflammatory diet may result in persistent low-grade inflammation. The dietary inflammatory index (DII) was enhanced to objectively assess the impact of food on inflammation [8]. Increased inflammatory cytokines have been found to cause a maternal immune reaction and this is associated with pregnancy complications [9, 10]. A pro-inflammatory diet, characterized by a high DII, may negatively impact fetal growth and elevate inflammatory markers in maternal serum [11]. Furthermore, oxidative stress is recognized to be pivotal in inflammatory disorders [12].

The current study aimed to examine the correlation between maternal DII, maternal circulating total oxidant status (TAS), total antioxidant status (TOS), interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF-α) levels in pregnant women diagnosed with FGR.

Materials and methods

Study population

This observational study encompassed pregnant women diagnosed with fetal growth restriction who were admitted to the Perinatology Clinic of Ankara Bilkent City Hospital for delivery between 2022 and 2023, with gestational ages ranging from 32 to 38 weeks ($n = 23$), alongside healthy pregnant women possessing identical demographic characteristics ($n = 23$). According to the power analysis performed on the sample article, the minimum number of patients was calculated to be 28, 14 in the study group and 14 in the control group with 80% power [13]. Pregnant women with chronic diseases such as chronic kidney disease, chronic liver disease, asthma, chronic hypertensive diseases, diabetes (gestational or pregestational) fetal anomalies, membrane ruptures, and multiple pregnancies were excluded from the study. In this study, according to the Delphi agreement, fetal abdominal circumference (AC) or estimated fetal weight (EFW) below the 10th percentile, accompanied by Doppler abnormalities, or either AC or EFW below the 3rd percentile without Doppler findings, validates the diagnosis of FGR [5].

Nutritional assessment and dietary inflammatory index (DII)

An expert dietitian (İ.S.G.) recorded the patients' dietary patterns. Dietary records were taken daily during the 3-day follow-up, two days on weekdays and one on the weekend, in order to include dietary changes, based on their frequencies of objective measurements such as cups and spoons, in order to minimize memory bias. Portion sizes of the consumed foods were assessed with the help of a photographic atlas to minimize recollection bias [14]. Active smoking and alcohol consumption were not included in this analysis because of their effects on the inflammatory and oxidative markers. In our study, the 3-day dietary recording period was designed to mitigate the potential impact of seasonal variations by ensuring that data collection was distributed across different times of the year. Additionally, participants who reported fasting or significant deviations from their usual diet (e.g., during holidays) were excluded from the analysis to minimize confounding effects. Research has shown that the dietary records performed similarly to web-based 24HDR ASA24, with both methods being more accurate

than food frequency, and fairly well compared to biomarkers in the assessment of energy, protein, potassium and sodium [15]. Daily energy and nutrient intakes were assessed using computer-based nutrition database software [(Ebispro for Windows, Stuttgart, Germany; Turkish Version (BeBiS 9) Istanbul Program uses data from Bundeslebensmittelschlussel (BLS) 3.01B and USDA-SR] [16]. The dietary intake of 29 food parameters, including energy, macronutrients (carbohydrate, protein, total fat, cholesterol, saturated fats, MUFAs, PUFAs, n-3, n-6 fats), fiber, caffeine, β-carotene, vitamins (C, A, E, D, B1, B2, B3, B6, folate, B12) and essential minerals (iron, zinc, magnesium, selenium), were used to calculate the Dietary Inflammatory Index [17]. Z-scores were computed utilizing a comprehensive database of means and SDs, normalized and multiplied with food parameter-specific scores to derive the total DII score. Elevated scores correlated with a more pro-inflammatory food pattern, whereas diminished scores indicated a more anti-inflammatory dietary pattern.

Biochemical evaluation

Evaluation of cytokine levels

Blood specimens were obtained from individuals and subjected to centrifugation at 3000 rpm for 5 min at 4 °C. Final supernatants were used for the measurement of cytokine, total antioxidant and oxidant levels. All measurements were determined spectrophotometrically using a UV-VIS Spectrophotometer (Epoch; BioTek, USA). The human TNF, IL-6, and IL-10 ELISA kits are an enzyme-linked immunosorbent assay for the quantitative detection of cytokine levels (e-BioSciences ELISA Ready SET-Go Affymetrix, Thermo Scientific). The capture antibody (100 ug/ml) was prepared in 1 ml phosphate-buffered saline (PBS) so that it would be 1 ug/ml, and 100 µL was added to each well of the high-affinity binding microwell plates. The plates were incubated for 16 h, then blocked with 200 µL of blocking solution. Samples and standards were added, incubated for 2 h, and then added to the plates. The detection antibody was added, and the plate was washed four times. Substrate solution was added, and the plate was incubated for 15 min. Stop solution was added and read in an ELISA reader at 450 nm. Standard curve ranges of TNF, IL-6, and IL-10 are evaluated and the detection limits of the kits were in the following order: TNF-α: 16–2500 pg/mL, IL-6: 30–2000 pg/mL, and IL-10: 15–1000 pg/mL.

Biochemical analysis of Oxidant / Antioxidant levels

Total antioxidant status (TAS), and total oxidant status (TOS) were measured with the spectrophotometric method by commercial kits (Rel Assay Kit Diagnostics, Turkey). Calculations are made by ΔAbs of standard or samples. Assay principle of the TAS measurement method depends on ABTS radical cation decolorization assay. The acetate buffer (0.4 mol/L pH: 5.8) and ABTS (30 mmol/l pH 3.6) are used as reagents. Antioxidants in a sample accelerate the bleaching rate proportional to their concentrations, measured time-dependently using spectrophotometry under 0.04 nm at 660 nm. The discoloration rate is inversely related to the Total Antioxidant Concentration (TAC). Trolox, a water-soluble vitamin E analog, calibrates the reaction rate. The TOS evaluations use a buffer solution and subtrate solution, based on the ferrous ion chelator complex to ferric ion in the samples. Assay methodology is based on the ferrous ion chelator complex to ferric ion in the samples. Hydrogen peroxide was used as a calibrator for TOS. The results were expressed in H_2O_2 equiv./L and concentration of standard units as µmol/L [18, 19].

Data analyses

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 26.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were employed to ascertain the demographic characteristics of the research individuals, including gestational age at labor, birth weight, DII, IL-6, IL-10, TNF-α, and TAS/TOS levels, which were compared across groups. The Kolmogorov-Smirnov and Shapiro-Wilk tests were employed to evaluate the normality of the distribution. Descriptive statistics, including mean ± SD, were utilized for the participants' fundamental characteristics, whereas demographic data were presented as median and minimum-maximum values. Relationships among continuous variables were examined using Pearson's correlation coefficients, while logistic regression analysis was conducted to ascertain the correlations between categorical variables and outcomes of interest. Furthermore, to assess the diagnostic efficacy, ROC curve analysis was performed, and the Youden index (J) was utilized to ascertain the best cut-off point of DII for predicting precision. The threshold for statistical significance was established at $p < 0.05$. All study protocols received approval from the Ethics Review Committee of Ankara City Hospital (No. E2-22-2948) and were executed in compliance with the Declaration of Helsinki. All participants submitted signed informed consent before enrolling in the study. Written informed consent forms included that the biological materials collected for the study would be safely stored and not used for any other purpose. This measure safeguards the privacy and rights of the participants, promoting trust in the research process. Additionally, all data collected will be anonymized to further safeguard patient confidentiality. This study was supported by the Turkish Health Institutes (TUSEB) (project no: 37268), which had no role in the study's design, data collection, analysis, interpretation, or manuscript preparation.

Table 1 Comparative analysis of mother's characteristics, daily nutritional consumption, and plasma cytokines and oxidative equilibrium

Variables	FGR	Control	*P* value
Age	27 (20–38)	*29 (21–41)*	0.782
Gravida	2 (1–8)	2 (1–5)	0.162
Parity	1 (0–2)	1 (0–4)	**< 0.001**
Abortus	0 (0–5)	0 (0–3)	0.999
Pre-Pregnancy BMI	24.6±4.8	26.6 ±5	0.166
Prior to Delivery BMI	28.6±5	30.7±5.1	0.183
Gestasional Age of Delivery	37.3±1.2	38.6±1.2	**< 0.001**
Weights of Delivery (Gram)	2456±282	3357±399	**< 0.001**
Dietary Inflammatory Index (DII)	3.44±2.2	-2.86 ± 5.5	**< 0.001**
Energy Intake (calori)	1799±195	2032±303	**0.004**
Protein Intake (gram)	62.9±10	72.7±14	**0.011**
Protein Intake %	14.3±2.2	14.7±2.8	0.602
Fat Intake (gram)	82.4±15.6	85±23.7	0.625
Fat Intake %	40.6±5.1	37.1±6.5	**0.05**
Saturated Fat Intake (mg)	34.2±8	34.7±14.7	0.876
Carbonhydrate Intake (gram)	197±30.4	236 ±47.6	**0.002**
Carbonhydrate Intake %	45±5.7	47.9±7	0.143
Cholesterol Intake (mg)	371±116	373±179	0.959
Fiber (gram/day)	16.15±3.73	27.08±6.28	**< 0.001**
TAS/TOS	0.05 ±0.02	0.06±0.03	0.362
TOS mmol/L	17.7±6.8	16.8±9.6	0.708
TAS mmol/L	0.76±0.2	0.82±0.2	0.364
TNF pg/mL	91.6 ±42.4	35.7±46.4	**< 0.001**
IL-10 pg/mL	82±39.1	123.1±91.3	**0.05**
IL-6 pg/mL	97.1±68.2	64.2±46.6	0.062

* Variables were shown as mean and standard deviation or median and interquartile range depending on the distribution of the data. BMI, body-mass index, DII, dietary inflammatory index, TAS, total oxidant status, TOS, total antioxidant status, IL-6, interleukim-6, IL-10 interleukin-10, TNF-α, tumor necrosis factor-alpha

Table 2 Regression analysis of factors associated with fetal growth restriction risk

Variables	Coefficient	Sig. (*p*-value)	Odds Ratio	95% CI Lower	95% CI Upper
Dietary Inflammatory Index	0.448	**0.001**	1.62	1.209	2.194
Energy Intake	-0.004	**0.009**	0.99	0.993	0.999
Carbonhydrate intake	-0.026	**0.006**	0.97	0.956	0.992
Protein intake	-0.096	**0.009**	0.91	0.845	0.976
Fat intake	0.013	0.648	1.013	0.957	1.072
Cholesterol intake	0.004	0.168	1.004	0.998	1.010
Pre-pregnancy BMI	-0.088	0.168	0.916	0.809	1.038
Prior to delivery BMI	-0.081	0.184	0.922	0.817	1.039

*BMI, body-mass index, DII, dietary inflammatory index

Results

The demographic data and clinical characteristics of the cases were summarized in Table 1. A significant increase in DII was observed in the study group ($p < 0.001$). The study group exhibited significantly lower energy ($p = 0.004$), carbohydrate ($p = 0.002$), protein ($p = 0.011$) and fiber ($p < 0.001$) intakes than the control group. Conversely, no statistically significant variation was observed in fat intake, particularly saturated fat and cholesterol intake. TNF-α levels were elevated in the FGR group ($p < 0.001$). IL-6 levels, although elevated in the FGR group, did not reach statistical significance ($p = 0.06$). The IL-10 levels were lower in the study group than in the control group ($p = 0.05$). Conversely, no statistically significant differences were observed in TAS, TOS and TAS/TOS levels between the groups. Logistic regression analysis demonstrated that elevated DII levels increased the probability of FGR by 62% [$p = 0.001$, CI (1.209–2.195)], and that the risk of FGR increased significantly with decreased energy, carbohydrate, and protein intake. The data are presented in Table 2. According to the correlation analysis, there was a positive correlation between IL-6 and TOS ($r = 0.297$, $p = 0.045$), a strong positive correlation between the DII and maternal serum TNF-α ($r = 0.375$, $p = 0.01$) and a strong negative correlation between birth weight and TNF-α (r=-0.478, $p < 0.001$) and DII (r=-0.446, $p = 0.002$). The data are presented in Table 3. When the ROC curve was drawn for the DII, AUC: 0.866 was determined. Figure 1. The optimal cutoff point for the DII was determined as 1.21 with 82% sensitivity and 79% specificity.

Discussion

In this study, DII was compared between late-onset FGR diagnosed pregnant women and healthy pregnant women, and significant differences were found between the inflammatory / anti-inflammatory markers in maternal serum and the nutrition type.

The main findings of the study revealed that the DII was significantly higher in pregnant women diagnosed with FGR, and a negative correlation was found between the DII and birth weight. Additionally, women with FGR were found to have diets that were low in energy, protein, and fiber intake. The study also highlighted that TNF-α levels were elevated in the serum of pregnant women with FGR, with a positive correlation between TNF-α levels and DII, as well as a negative correlation between TNF-α levels and birth weight. However, no significant differences were observed between the groups in terms of IL-6 levels or TAS/TOS.

Inflammation has been associated with the etiology of numerous diseases, including cancer, dementia, hypertension, and insulin resistance. In recent years, the DII has been established to objectively illustrate the impact

Table 3 Correlations between inflammatory and anti-inflammatory markers, oxidative stress indicators, dietary inflammatory index (DII), and birth weight

Corelations	IL6		IL10		TNF		TAS		TOS		TAS/TOS		DII	
	Pearson	P value	Pearson	P value	Pearson	P value	Pearson	P value	Pearson	P value	Pearson	P value	Pearson	P value
IL-6 pg/mL			0.097	0.521	0.082	0.587	0.074	0.627	0.297*	**0.045**	−0.106	0.481	0.160	0.287
IL-10 pg/mL	0.097	0.521	1		−0.097	0.521	−0.030	0.843	0.021	0.889	0.278	0.062	−0.237	0.112
TNF pg/mL	0.082	0.587	−0.097	0.521	1		−0.078	0.604	0.085	0.572	−0.163	0.278	0.375*	**0.010**
TAS mmol/L	0.074	0.627	−0.030	0.843	−0.078	0.604	1		−0.011	0.940	0.411**	**0.005**	0.082	0.590
TOS mmol/L	0.297*	**0.045**	0.021	0.889	0.085	0.572	−0.011	0.940	1		−0.680**	**0.000**	0.018	0.907
TAS/TOS	−0.106	0.481	0.278	0.062	−0.163	0.278	0.411**	**0.005**	−0.680**	**0.000**	1		−0.007	0.964
Dietary Inflammatory Index	0.160	0.287	−0.237	0.112	0.375*	**0.010**	0.082	0.590	0.018	0.907	−0.007	0.964	1	
Birth weight	−0.211	0.158	0.235	0.116	**−0.478**	**<0.001**	0.266	0.074	0.037	0.806	0.145	0.335	**−0.446**	**0.002**

1. *$p<0.05$, **$p<0.01$: Indicates statistically significant correlations

2. Pearson correlation coefficient is reported for the relationships between the variables

DII, dietary inflammatory index, TAS, total oxidant status, TOS, total antioxidant status, IL-6, interleukin-6, IL-10 interleukin-10, TNF-α, tumor necrosis factor-alpha

of nutrition on inflammation, spanning a continuum from proinflammatory to anti-inflammatory [8]. The DII is deemed positive if the nutrient has an inflaming effect and negative if it demonstrates an anti-inflammatory effect. A study conducted in the USA reported that a high BMI prior to pregnancy was associated with higher levels of DII and CRP, and that babies born to these mothers were more likely to be diagnosed with FGR [11]. Although there was no significant difference between the BMI of the control and study groups in this study, the study revealed that the DII was significantly elevated in the FGR group, with a very significant negative connection between the DII and birth weight. This outcome aligns with other research findings. A 2023 study in China shown that elevated DII scores correlate with reduced baby weight, premature birth, and congenital anomalies [20]. This indicates that an inflammatory diet elevates the likelihood of fetal growth restriction and is strongly correlated with birth weight. However a recent study evaluating the impact of DII on fetal growth patterns indicated that proinflammatory diet might be associated with both FGR and large for gestational age (LGA). Although, the hypothesis of the mentioned study had similarities with the present study, there were main differences like higher number of obese/overweight participants, a large range for DII values, absence of other inflammatory markers and the investigation of pregnant women between 24-39th weeks of gestation [21].

In the present study, macronutrient intake of participants was also examined. Macronutrients are nutrients that must be consumed in large amounts daily to provide the energy required to maintain body functions [22]. Upon evaluation of the groups, no significant changes were noted in pre-pregnancy and pre-delivery BMI; however, caloric intake, consumption of carbohydrates, and protein intake were considerably reduced in the FGR group. Despite no notable variation in fat consumption across the groups, the proportion of dietary fat consumed was markedly greater in the FGR group. No significant variations were observed in saturated fat or intake of cholesterol when fat consumption was analyzed in depth.

These results suggest that adequate daily energy intake, adequate protein intake, and balanced fat intake may protect against FGR development. The present study examined dietary fiber intake in pregnant women. Adequate fiber intake balances glucose and insulin levels and acts as a powerful anti-inflammatory prebiotic that alters intestinal microbiota and microbial metabolism [23]. A notable observation was the low fiber intake documented in the cohort of women diagnosed with FGR. These findings suggest that a diet consisting of low-glycemic index grains (e.g., coarse cracked wheat, quinoa, brown rice), vegetables (e.g., cabbage, spinach, beans, peas, lentils),

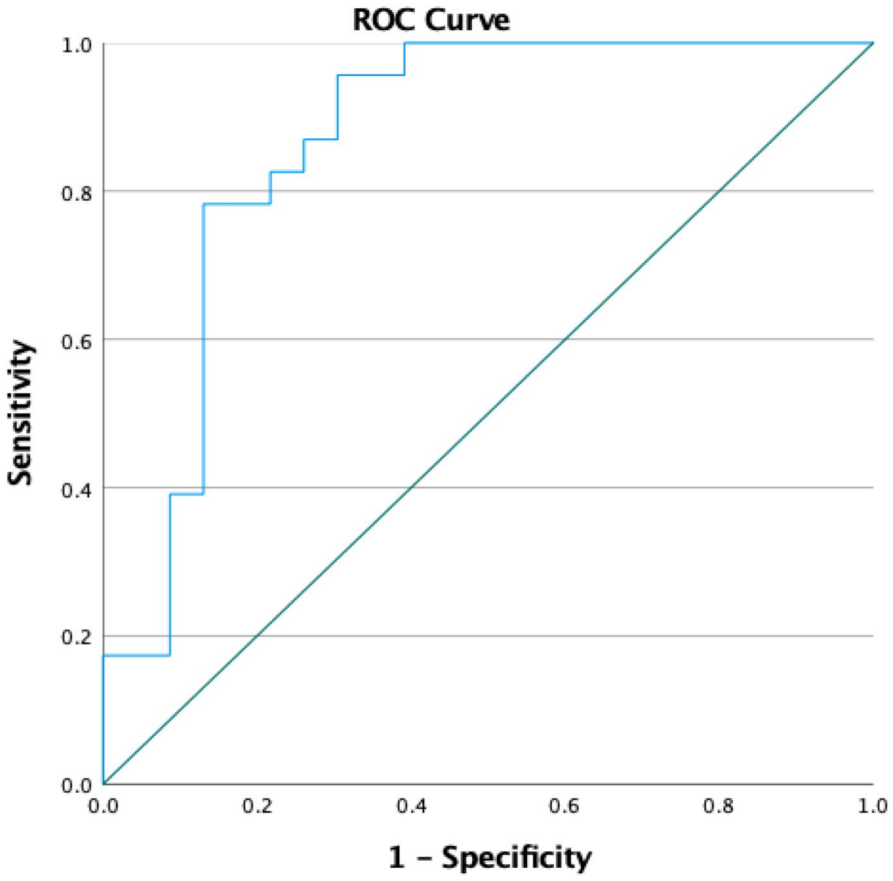

Fig. 1 ROC curve analysis to evaluate the diagnostic performance of dietary inflammatory index for fetal growth restriction. *Area under the curve (AUC) value is 0.866

and fruits (e.g., apples) may contribute to a reduced risk of developing FGR.

Hébert et al. examined the impact of the inflammatory potential of foods on health, revealing that a high dietary inflammatory index exerts a pro-inflammatory effect by modulating the levels of inflammatory and anti-inflammatory cytokines (IL-1β, 4, 6, 10, TNF-α) and CRP, while a low dietary inflammatory index demonstrates an anti-inflammatory effect [24]. A further study indicated that a diet rich in saturated fats, refined grains, and simple carbs was associated with elevated levels of CRP and IL-6 [25].

Inflammatory cytokines such as TNF-alpha and IL-6 are necessary for maternal vascular and decidual invasion during implantation. However, from the second trimester onwards until delivery, an anti-inflammatory environment is required for the healthy development of the fetus. If this anti-inflammatory environment cannot be established, pregnancy complications such as preeclampsia, preterm labor, and preterm premature rupture of membranes (PPROM) may be occur [26]. In other studies that examined inflammatory markers in maternal serum to demonstrate the relationship between FGR and sterile inflammation of the placenta, higher levels of IL-6 and TNF-α were reported in the FGR group [27]. Some studies have suggested that trophoblastic hypoxia and protein-poor low-calorie diets may play a role in increasing IL-6 production by peripheral blood mononuclear cells [28]. One study reported elevated plasma IL-6 levels in pregnant women diagnosed with FGR between 25 and 35 weeks of gestation [27].

Conversely, it has been shown that IL-6 levels decrease in the cord blood after birth in low-birth-weight newborns. However, IL-6 remains a significant biomarker for identifying postnatal hypoxia [29]. Significant difference was not found between the groups for IL-6 in the current study. The observed discrepancy in IL-6 levels, in contrast to the findings reported in most studies, may be attributable to the participation of pregnant women who had reached 32 weeks of gestation, had no cases of very low birth weight, and were delivered in a hospital setting without experiencing hypoxic conditions.

Similarly, the levels of TAS/TOS did not differ significantly between groups, indicating that oxidative balance is an indirect marker of hypoxia. Some studies report that women diagnosed with FGR experience oxidative

stress, particularly those with hypertension [30, 31]. Others indicate oxidative damage in both underweight and large for gestational age (LGA) fetuses [32] or found no changes in FGR pregnancies [33]. In addition to the conflicting results in the literature, the absence of significant differences in this study may be attributed to some factors such as interventions prior to the development of hypoxia and selection of normotensive patients in the study group. Another finding of this study is the significant positive correlation between IL-6 and TOS, suggesting that both markers may tend to increase due to hypoxia.

The inflammatory marker TNF-α was significantly raised in the study group, while the anti-inflammatory agent IL-10 was dramatically lowered in pregnant women who were diagnosed with FGR. A positive and significant connection was found amongst maternal TNF-α and DII scores. This data indicates a substantial correlation between TNF levels and DII, highlighting the possibility for food to directly modulate TNF expression. TNF-α is a significant inflammatory marker that is essential in various physiological processes, including folliculogenesis, embryogenesis, conception, and parturition. Previous investigations identified higher levels of TNF-α throughout the final trimester of pregnancy, suggesting that TNF-α may be implicated in parturition. Moreover, elevated levels of TNF-α have been observed in pregnant women who have undergone recurrent abortion, premature rupture of membranes, preeclampsia, and fetal growth restriction (FGR) [34]. Furthermore, increased TNF-α and reduced IL-10 levels have been noted in pregnant women who were diagnosed with FGR [35]. In a study in which placentas from normal-weight fetuses and fetuses with FGR were examined immunohistochemically, increased TNF-alpha tissue expression was reported in placentas of fetuses with FGR [36]. As a result of the toxic effect of TNF-alpha on the endothelium and its ability to cause placental thrombosis, it is thought that it causes inadequate perfusion of the uteroplacental bed and predisposes to FGR [37, 38]. A separate investigation indicated a connection between increased DII and TNF-α levels [39]. One of the main hypothesis for FGR is excessive inflammation in the maternal-fetal interface resulting in insufficient perfusion to the developing fetus. We believe that diet of pregnant women may affect basal inflammation in the maternal-placental unit and TNF-a may reflect this inflammation.

IL-10 is classified as an anti-inflammatory cytokine. Studies have associated high DII levels with low IL-10 levels in pregnant women [40]. Studies have shown that IL-10 expression is reduced in the placenta of pregnant women diagnosed with FGR [41]. The present study confirms the findings of previous studies. Maternal pro-inflammatory diet has been shown to elevate inflammatory cytokines and reduce anti-inflammatory substances in maternal serum. Consequently, an atmosphere favorable to the advancement of FGR is established.

The present study has the following limitations: challenges in recalling the daily dietary record throughout DII interviews, small sample size, the absence of a longitudinal design, the cross-sectional study design, unmeasured cofactors such as pollution, genetic variations of inflammation pathways, stress levels, access to healthcare and the focus solely on pregnant women receiving a diagnosis of late-onset FGR. Conversely, the interdisciplinary approach, the inclusion of pregnant women who were diagnosed with isolated FGR, and the simultaneous evaluation of DII, cytokines, and TAS/TOS are significant attributes of this study.

Conclusion

The findings of the present study indicate that a pro-inflammatory diet may be associated with an increased risk of FGR. Individualized management of obstetric complications has been a rising trend in maternal-fetal medicine. Thus, healthy dietary habits should be an important part of perinatal care. Consequently, even if altering dietary habits may reduce the likelihood of developing FGR, as well as perinatal neonatal mortality and morbidity, it is important to acknowledge that the study design does not allow for definitive conclusions regarding causality. Further population-based research using larger sample sizes is required to investigate the impact of nutrition on pregnancy-related problems.

Abbreviations

FGR	Fetal growth restriction
DII	Dietary Inflammatory Index
TOS	Total Oxidant Status
TAS	Total Antioxidant Status
IL-6	Interleukin-6
IL-10	Interleukin-10
TNF-α	Tumor Necrosis Factor-Alpha
SPSS	Statistical Package for the Social Sciences

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None.

Author contributions

Ayşe Gülçin Baştemur and İclal Sena Gezer collected the patients' data and maternal serums. Atakan Tanaçan and Özgür Kara were responsible for the study design, statistical analyses. Burcu Kesikli and Nuray Yazıhan made biochemical analyses of the materials collected. Ayşe Gülçin Baştemur wrote the manuscript, while Dilek Şahin reviewed the study.

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Data availability

The datasets generated and analysed during the current study are not publicly available due to ethical and legal regulations in Turkey but are available from the corresponding author on reasonable request.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
All study protocols received approval from the Ethics Review Committee of Ankara City Hospital (No. E2-22-2948) and were executed in compliance with the Declaration of Helsinki. All participants submitted signed informed consent before enrolling in the study.

Consent for publication
There are no circumstances in the study that violate anonymity, and identifying information has been kept confidential. There are no issues regarding its publication.

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