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Prenatal irisin is inversely related to the term placental telomere length

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Abstract

Irisin is a myokine mainly produced by skeletal muscle that impacts the body's systemic metabolism. It is connected to aging, telomere length, and oxidative stress markers in human adults and in vitro. The serum irisin concentration increases during pregnancy and has been linked to some birth outcomes like macrosomia. On the other hand, its inverse relation with the chance of pregnancy disorders like preeclampsia and gestational diabetes suggests a protective role for this myokine in pregnancy. It is suggested that irisin may exert its impact on pregnancy by affecting the placenta, which has not been studied yet. Here, we questioned whether prenatal serum irisin is related to placental markers, including telomere length and antioxidant activity. Research has shown that the status of these markers at birth can predict the predisposition to some chronic diseases later in life.
We included 80 pregnant mothers (17–41 years old) and newborn dyads randomly selected from the enrolled participants of the Rafsanjan Birth Cohort Study (one of the five district areas of the PERSIAN birth cohort studies), who delivered at the Nik-Nafs Maternity Hospital in Rafsanjan in 2022. Irisin levels were measured in the mother's blood serum in pregnancy using ELISA. The relative telomere length and the GPX and SOD enzyme activities were measured in the term placenta using real-time PCR and colorimetric assays, respectively. We found an inverse relationship between the serum irisin levels during pregnancy and relative telomere length in the term placenta. Irisin level was not significantly associated with the activity of SOD and GPX enzymes. Therefore, our data does not support the protective role of prenatal irisin on the placental telomere shortening and oxidative stress. Future studies are warranted to assess more placental markers in relation to pregnancy irisin levels.

Keywords Irisin, Prenatal, Placenta, Telomere, Oxidative stress

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Introduction

Irisin consists of 112 amino acid residues and is synthesized and released by skeletal muscles following exposure to cold and exercise. This hormone is produced by the activation of peroxisome proliferator-activated receptor-γ coactivator 1 (PGC-1α) and proteolytic cleavage of fibronectin type III domain-containing 5 (FNDC5). Irisin is believed to function as an intermediary between skeletal muscle and various other tissues involved in energy regulation and metabolism [1]. During human pregnancy, the concentration of irisin increases. In pregnancy disorders like preeclampsia [2] and gestational diabetes [3], a decrease in circulating irisin levels is reported in comparison to healthy individuals, suggesting a protective role of irisin against these pregnancy complications. Conversely, another human study revealed a correlation between the increasing levels of irisin during the initial trimester of pregnancy and the possibility of macrosomia as an adverse birth outcome [4]. Therefore, there is controversy in understanding the role of irisin in pregnancy since it has been linked to both adverse birth outcomes and protection against some pregnancy or birth complications.

The placenta is a unique organ that serves multiple functions in facilitating communication between the mother and the fetus [5]. To maintain its proper physiological function, the placenta requires energy, which is obtained through mitochondrial oxidative phosphorylation. Therefore, the placenta is exposed to oxidative stress resulting from mitochondrial activity [6–9]. In vitro studies have suggested the impact of irisin on placental control of oxidative stress and trophoblast differentiation [10, 11]. However, to our knowledge, no in vivo human studies have assessed the placental status in relation to irisin levels during pregnancy.

Telomere shortening in tissues is an indication of DNA damage induction and poor stress response [12]. Shorter placental telomere length has been attributed to placenta aging and oxidative stress and is shown to be associated with adverse pregnancy outcomes such as preeclampsia, gestational diabetes, and intrauterine growth restriction [13–18]. In addition, recent research studies suggest that the status of some markers like telomere length at birth could potentially predict lifespan and vulnerability to age-related diseases during adulthood [19]. Research conducted on the effect of irisin on one generation (in adults) suggests that there is a significant correlation between circulating irisin levels and telomere length, indicating that irisin may impact aging [20]. To date, no study has examined the transgenerational impact of irisin levels. The present study aimed to examine the connection between maternal serum irisin levels during pregnancy and term placental markers, including telomere length and the activity of superoxide dismutase and glutathione peroxidase as frequently used markers to assess the capacity to eliminate radicals generated by oxidative stress. Our goal is to ask whether irisin induction in pregnancy may be a mechanism to protect the placenta against oxidative stress and telomere shortening.

Materials and methods

Recruitment of participants, data collection, and ethics

Considering a correlation of 0.33 between irisin and telomere length in adults [20], a power of 80%, and an alpha level of 0.05, a sample size of 70 pairs (mother-infant) was calculated. Primarily, we included 80 pregnant mothers (17–41 years old) and their offspring from the enrolled participants of the Rafsanjan Birth Cohort Study (1423 participants), who delivered at the Nik Nafs Maternity Hospital in Rafsanjan from April To November 2022. The mothers' first-trimester blood serum and their neonates' term placenta samples were collected. Rafsanjan is one of the five Iranian cities participating in the PERSIAN Birth Cohort study [21]. Participants of our current cross-sectional study had to be of Iranian nationality and provide written consent. Inclusion criteria were pregnant mothers who did not have maternal pre-pregnancy BMI exceeding 30 kg/m^2, gestational diabetes, thyroid disorders, or hypertension in pregnancy, and use of tobacco, alcohol, or drugs. Exclusion criteria for this work were the presence of gestational diabetes, thyroid disorders, or hypertension in pregnancy diagnosed after the first-trimester blood collection, incomplete information and questionnaires, clots or other problems in the blood or placental samples, premature birth of the neonate, and any other pregnancy and birth complications. Fortunately, no maternal or neonate morbidity occurred among our cases of study. Finally, 70 mothers-newborn pairs were entered into analyses.

All the invitations, interviews, measurements, and physical examinations conducted in the Rafsanjan birth cohort study were carried out under the close supervision of the Iranian Ministry of Health and Medical Education, as well as the PERSIAN Birth Cohort Central Committee, in strict adherence to the PERSIAN birth cohort's protocol [21]. Additionally, the study protocol was approved by the ethics committee of Rafsanjan University of Medical Sciences (Code of Ethics: IR.RUMS.REC.1401.105). All participants of the PERSIAN birth cohort study undergo comprehensive interviews, physical examinations, and biological sample donations, followed from early pregnancy to giving birth. Comprehensive data is collected for each participant, including socio-demographic background, physical activity and lifestyle factors, detailed delivery conditions, pregnancy-related complications, pregnancy outcomes, and detailed information on neonate examination.

DNA extraction and telomere length measurements

Using the SinaPureTM DNA kit (Cinaclon, DNeasy Cell culture, Tissue, Gram-negative bacteria, and Csf Kit), we followed the manufacturer's instructions to extract around 100 micrograms of genomic DNA from placental tissues. Next, we utilized real-time polymerase chain reaction (PCR) to determine the relative telomere length of the DNA samples from the placental tissues. This involved measuring the telomeric repeat copy number (T) in relation to the copy number of a nuclear single copy gene (36B4d) (S) within each sample, expressed as a T/S ratio. We then used this ratio to evaluate the relative telomere length (RTL) compared to a standard DNA sample included in each PCR run [22]. We carried out the PCR runs in triplicate using an Applied Biosystems step one plus Real-Time PCR machine and BIOSYSTEM Syber Green Mix qPCR reagent. See supplemental Table 1 for primer sequences.

Assessment of the activity of antioxidant enzymes

The placental tissues were fragmented into small pieces, and 100 mg of the frozen placenta was homogenized in 1 ml of ice-cold PBS buffer (100 mM, pH 7.4) using a homogenizer. The resulting mixture was then centrifuged at 6000 rpm for 20 min at 4 °C, and the supernatant was separated and stored in sterile microtubes at -80 °C. Activity levels of antioxidant enzymes superoxide dismutase (SOD) and glutathione peroxidase (GPX) were assessed using commercially available colorimetric assays following the manufacturer's instructions (ZellBio, Germany).

Irisin measurement

The level of maternal irisin was measured in blood serum by enzyme-linked immunosorbent assay (ELISA), following the instructions provided by the kit manufacturer (ZellBio, Germany).

Statistical analysis

Quantitative variables were described by either presenting the mean ± standard deviation or median as appropriate, while categorical variables were presented as frequency and percentage. The chi-square or Fisher exact test was used for categorical variables, and the independent t-test was used for normally distributed quantitative variables. Since the dependent factors (relative telomere length and activity of SOD or GPX enzymes) did not have a normal distribution among our study population, the median value for each of the abovementioned factors in the study subjects was used as the cutoff value: values greater than or equal to the telomere length median were considered high levels of relative telomere length, and values below the median were considered low levels of relative telomere length. Values greater than or equal to the median of SOD or GPX activity were named high levels of SOD or GPX activity, and values below the median were taken as low levels of SOD or GPX activity.

We used both crude and adjusted logistic regression analyses to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the associations between maternal irisin levels and relative telomere length, GPX antioxidant enzyme activity level, or SOD antioxidant enzyme activity level. The potential confounding factors tested in our analysis include maternal weight before and during pregnancy, the mother's age, passive smoking, educational background, and various birth and newborn factors such as newborn gender, weight at birth, gestational age at birth, and the type of delivery, selected based on the relevant literature and subject matter knowledge. The confounder variables selected and included in the analysis were the neonate's weight, neonate's gender, gestational age, mother's education, mother's weight before pregnancy, and passive smoking. To select the confounders, separate models at the bivariate level were used to obtain variables that were related to telomere length, GPX enzyme activity, and SOD enzyme activity. For this purpose, variables with a p-value of less than 0.25 in the bivariate model (based on Hosmer and Lemeshow [23, 24]), as well as parameters that were recognized by the literature to be effective on the dependent variable, were included in the multivariable model as confounders. All analyses were conducted by STATA V.14. We considered p-values to be two-sided, and p-values < 0.05 and 95% confidence intervals not including one were considered statistically significant.

Results

In the present cross-sectional study, out of 80 Iranian mothers, ultimately, 70 mothers were included in the study after applying the exclusion criteria explained in the methods. Irisin concentration was measured in maternal blood serum at the end of the first pregnancy trimester. Next, the following parameters were measured in the term placenta, the relative telomere length, and placental GPX and SOD enzyme activities (Table 1). The relationship between the abovementioned parameters and the hormone irisin in the serum of the mother was then evaluated.

Descriptive results

No significant difference in the mean irisin level (p-value = 0.36) was observed between the telomere_high and telomere_low groups (Table 2). According to Table 3, no significant difference was found in the mean irisin hormone level (p-value = 0.69) between the two GPX_low and GPX_high groups. No significant association was observed between SOD enzyme activity level and the mean irisin hormone level (p-value = 0.97) (Table 4).

Table 1 Baseline characteristics of the study population

Median (IQR)	
RTL	5.45 (7.68)
SOD activity (U/mg)*	6.35 (2.69)
GPX activity (U/mg)*	115.41 (187.54)
Mean ± SD	
Maternal Irisin (ng/ml)	18.81 (1.82)
Neonate weight (kg)	3122.31 (380.04)
Neonate height (cm)	48.66 (2.52)
Neonate head circumference (cm)	34.18 (1.13)
Gestational age (week)	38.91 (1.19)
Mother age at childbirth (year)	29.96 (5.77)
Number (%)	
Mother Second-hand smoking in pregnancy (%)	
yes	14 (17.07)
no	68 (82.93)
Mother university education (%)	
yes	28 (33.73)
no	55 (66.27)
Neonate gender (%)	
Boy	34 (45.95)
Girl	40 (54)
Delivery type (%)	
Natural	34 (45.95)
Cesarean	40 (54.05)

Data are presented as mean ± SD (Standard deviation), or an absolute number n (percentage)

IQR: interquartile range

RTL: relative telomere length

*Units of enzyme activity in 1 mg of the placental tissue protein extract

Logistic results

To investigate the association between the relative telomere length and maternal serum irisin level, logistic regression models were used, including crude and multivariate models. In the adjusted model 1, the effects of newborn gender, birth weight, and gestational age were adjusted for, and in model 2, in addition to the variables in adjusted model 1, maternal education [25–27], maternal age [28], and passive smoking [29] were also included due to the literature reports on their biological impact on the neonate's telomere length, and for maternal education and passive smoking, our observation of a p-value < 0.250 in the bivariate regression test.

As shown in Table 5, in the univariate model, no significant association was observed between relative telomere length and maternal serum irisin level (OR: 0.84, 95%CI = 0.59–1.20, p-value = 0.35). However, in the adjusted model 1, a significant inverse association was observed between serum irisin level and the placental relative telomere length, and the association was such that with an increase in irisin level, the odds of being telomere_high compared to the telomere_low decreased (OR = 0.50, 95%CI = 0.27–0.94, p-value = 0.03). Also, in adjusted model 2, a significant inverse association was observed (OR = 0.47, 95%CI = 0.23–0.96, p-value = 0.04). Figure 1 represents the association graph of adjusted model 2, indicating the negative direction of association between serum irisin and the placental telomere length.

To investigate the association between GPX activity and maternal serum irisin level, in the adjusted model 1, the effects of newborn gender, newborn birth weight, and gestational age were moderated, and in adjusted model 2, in addition to the variables in adjusted model 1, maternal education and pre-gestational weight, and maternal age were also included as cofounders. No significant association was observed in the unadjusted model (OR = 0.92, 95%CI = 0.63–1.34, p-value = 0.69), adjusted model 1 (OR = 0.95, 95% CI = 0.60–1.49, p-value = 0.83), and adjusted model 2 (OR = 1.17, 95%CI = 0.59–2.29, p-value = 0.64) between the GPX activity and serum Irisin (Table 5).

In respect to the association between SOD activity and maternal serum irisin level, in the adjusted model 1, the effects of newborn gender, newborn birth weight, and gestational age were moderated, and in adjusted model 2, in addition to the variables in adjusted model 1, maternal education, maternal age and passive smoking were also adjusted for. No significant association was observed in the crude model (OR = 1.00, 95%CI = 0.74–1.35, p-value = 0.97), adjusted model 1 (OR = 0.99, 95%CI = 0.69–1.42, p-value = 0.98), and adjusted model 2 (OR = 1.05, 95%CI = 0.72–1.54, p-value = 0.77) between the serum irisin level and SOD activity (Table 5).

Discussion

The irisin hormone has been briefly associated with aging and oxidative stress markers in human adults and in vitro [20, 30, 31]. During pregnancy, the concentration of serum irisin increases and has been correlated with certain birth outcomes like preeclampsia, macrosomia, and gestational diabetes [2–4]. There is a suggestion that its impact may be exerted through its effect on the placenta. Here, we investigated some placental markers in relation to prenatal serum irisin levels and sought to determine if pregnancy irisin may be associated with higher protection of the placenta against oxidative stress and placental telomere shortening. In general, our data did not confirm the hypothesis, and we observed an inverse relationship between 1st-trimester blood serum irisin and term placental telomere length and found no association with the placental antioxidant activity of SOD and GPX.

Telomere shortening may indicate DNA damage and poor stress response in a tissue [12]. Based on our results, we may propose that a shorter placental telomere length associated with higher maternal irisin levels may indicate a negative impact of high irisin early in pregnancy connected to induced DNA damage in the placenta. We suggest future studies that investigate more comprehensively

Table 2 Baseline characteristics of the study population categorized by the relative telomere length

	RTL_low	RTL_high	*P*-value	Total
Neonate Sex (%)			0.68*	
Female	15(55.56)	14(50.00)		29(52.73)
Male	12(44.44)	14(50.00)		26(47.27)
Maternal education level (%)			0.34*	
Non-university	21(72.41)	17(60.71)		38(66.67)
University	8(27.59)	11(39.29)		19(33.33)
Delivery type (%)			0.66*	
Natural	10(37.04)	12(42.86)		22(40.00)
Cesarean	17(62.96)	16(57.14)		33(60.00)
Passive smoking (%)			0.08*	
Yes	3(10.34)	8(28.57)		11(19.30)
No	26(89.66)	20(71.43)		46(80.70)
Mean ± SD				
Gestational age (week)	38.94 ± 1.04	38.62 ± 1.39	0.34**	
Maternal irisin level	18.76 ± 1.56	18.26 ± 1.95	0.36**	
Neonate weight (g)	3294.16 ± 374.74	3004.81 ± 373.96	0.008**	
Neonate height (cm)	49.35 ± 1.27	48.03 ± 1.97	0.007**	
Neonate head circumference (cm)	34.48 ± 1.05	34.07 ± 1.07	0.17**	
Mother age (years)	31.58 ± 6.02	29.42 ± 5.22	0.15**	
Pre-gestational weight (kg)	70.73 ± 10.75	67.7 ± 16.33	0.48**	

Data are presented as mean ± SD (Standard deviation), or an absolute number n (percentage)

* Fisher Exact Test /χ^2 test

** t-test

RTL: relative telomere length

Table 3 Baseline characteristics of the study population categorized by the level of GPX enzyme activity

	GPX_low	GPX _high	*P*-value	Total
Neonate Sex (%)			0.77*	
Female	14(56.00)	15(60.00)		29(58.00)
Male	11(44.00)	10(40.00)		21(42.00)
Maternal education level (%)			0.09*	
Non-university	14(53.85)	19(76.00)		33(64.71)
University	12(46.15)	6(24.00)		18(35.29)
Delivery type (%)			0.56*	
Natural	12(48.00)	10(40.00)		22(40.00)
Cesarean	13(52.00)	15(60.00)		28(56.00)
Passive smoking (%)			0.39*	
Yes	4(15.38)	6(25.00)		10(20.00)
No	22(84.62)	18(75.00)		40(80.00)
Mean ± SD				
Gestational age (Week)	38.94 ± 1.30	38.9 ± 1.19	0.91**	
Maternal irisin level	18.83 ± 2.01	18.62 ± 1.47	0.69**	
Neonate weight (g)	3019.6 ± 291.67	3273.18 ± 444.57	0.02**	
Neonate height (cm)	48.36 ± 2.14	48.68 ± 3.55	0.70**	
Neonate head circumference (cm)	33.98 ± 1.14	34.52 ± 1.14	0.10**	
Mother age (years)	30.80 ± 4.81	30.64 ± 7.02	0.92**	
Pre-gestational weight (kg)	61.88 ± 12.34	70.29 ± 12.96	0.03**	

Data are presented as mean ± SD (Standard deviation), or an absolute number n (percentage)

* Fisher Exact Test /χ^2 test

** t-test

Table 4 Baseline characteristics of the study population categorized by the level of SOD enzyme activity

	SOD_low	SOD_high	*P*-value	Total
Neonate Sex (%)			0.45*	
Female	16(48.48)	19(57.58)		35(53.03)
Male	17(51.52)	14(42.42)		31(46.97)
Maternal education level (%)			0.87*	
Non-university	22(64.71)	22(62.86)		44(63.77)
University	12(35.29)	13(37.14)		25(36.23)
Delivery type (%)			0.62*	
Natural	16(48.48)	14(42.42)		30(45.45)
Cesarean	17(51.52)	19(57.58)		36(54.55)
Passive smoking (%)			0.04*	
Yes	9(27.27)	3(8.57)		12(17.65)
No	24(72.73)	32(91.43)		56(82.35)
Mean ± SD				
Gestational age (Week)	38.81 ± 1.33	38.98 ± 1.15	0.59**	
Maternal irisin level	18.79 ± 2.17	18.81 ± 1.46	0.97**	
Neonate weight (g)	3132.58 ± 403.58	3085.60 ± 317.70	0.61**	
Neonate height (cm)	48.43 ± 2.14	48.59 ± 2.88	0.80**	
Neonate head circumference (cm)	34.22 ± 1.16	34.16 ± 1.08	0.83**	
Mother age (years)	30.08 ± 6.44	29.68 ± 5.13	0.77**	
Pre-gestational weight (kg)	68.9 ± 17.56	64.57 ± 10.99	0.27**	

Data are presented as mean ± SD (Standard deviation), or an absolute number n (percentage)

* Fisher Exact Test /χ^2 test

** t-test

Table 5 Estimated unadjusted and adjusted odds ratios for maternal irisin level, as predicted by relative telomere length, GPX antioxidant enzyme activity, and SOD antioxidant enzyme activity

	Crude model			Adjusted Model 1			Adjusted Model 2		
	OR(95% CI)	p-value	Pseudo R^2	OR(95% CI)	p-value	Pseudo R^2	OR(95% CI)	*p*-value	Pseudo R^2
Long RTL	0.84(0.59–1.20)	0.35	0.014	0.50(0.27–0.94)	0.03*	0.261	0.47(0.23- 0.96)	0.04**	0.330
High GPX	0.92(0.63–1.34)	0.69	0.003	0.95(0.60–1.49)	0.83*	0.070	1.17(0.59- 2.29)	0.64***	0.289
High SOD	1.00(0.74–1.35)	0.97	< 0.001	0.99(0.69–1.42)	0.98*	0.021	1.05(0.72- 1.54)	0.77****	0.071

OR: odd ratio, CI: confidence interval

* Adjusted for neonate gender, neonate weight, gestational age

** Adjusted for neonate gender, neonate weight, gestational age, Mother's education, passive smoking, and maternal age

*** Adjusted for neonate gender, neonate weight, gestational age, Mother's education, Pre-gestational weight, and maternal age

**** Adjusted for neonate gender, neonate weight, gestational age, Mother's education, passive smoking, and maternal age

the status of irisin and other myokines and adipokines in pregnancy in relation to placental DNA damage, oxidative stress, and stress response mechanisms to gain a better understanding of the physiology of pregnancy and placenta affected by these endocrine factors. Telomere length becomes shorter due to cell division and DNA damage induced by environmental factors [12, 32–34]. Its size can be elongated and maintained by telomerase activity. In most differentiated cells, telomerase activity is absent. Therefore, the telomere length in a cell is defined by the number of cell divisions before cell differentiation and by the level of telomerase activity [32]. In placental development, the telomerase activity is highest in the first trimester [35]. Since irisin is shown to induce trophoblast differentiation [10], one may speculate that the consequent abrogation of the telomerase activity following cell differentiation may be the underlying mechanism of shorter telomere length we observed in placenta associated with higher maternal irisin levels. This hypothesis remains to be assessed in future analysis, measuring the level of DNA damage, DNA damage response mechanisms, and telomerase activity in the placenta in relation to the level of serum irisin. Also, studies with larger population sizes are required to include more exposure variables in their analyses, such as the nutritional status of the mother during pregnancy.

Irisin secretion is known to be mainly induced by muscle contraction and exercise [36]. Therefore, our study may present preliminary results pointing to some potentially negative impacts of exercise during the first trimester of pregnancy. Future studies are warranted to test this

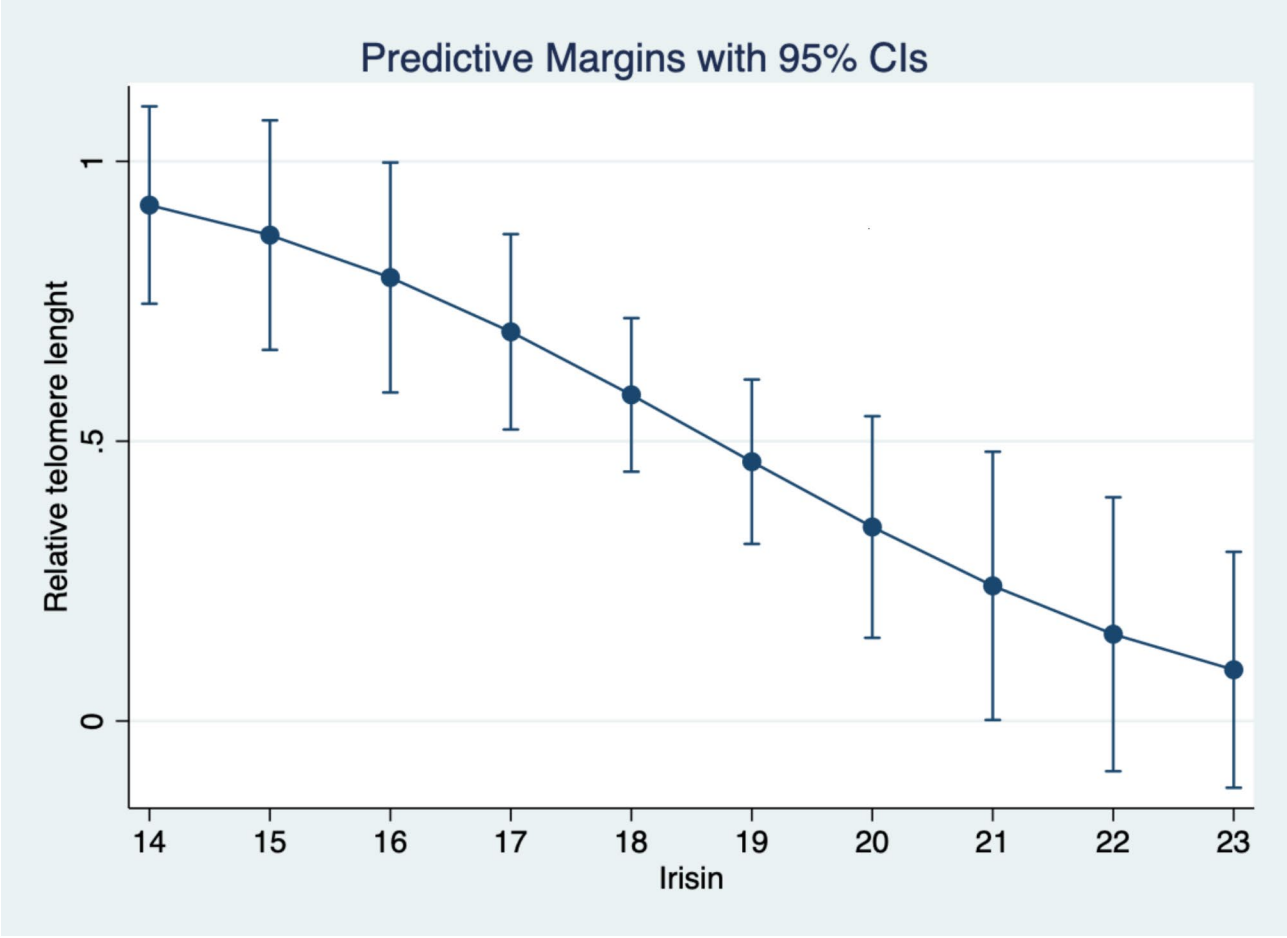

Fig. 1 Graphic representation of the adjusted association between maternal serum irisin and the term placental relative telomere length

hypothesis in larger samples, including the assessment of more health-related markers in the placenta.

Three previous studies in different experimental settings have investigated the link between irisin and telomere length. In 2014, a group studying 81 healthy adults found a positive correlation between serum irisin and blood mononuclear cells' telomere length [20]. In 2017, the same group reported a nonsignificant negative correlation between serum irisin and leukocyte telomere length in 79 adult type 2 diabetic patients [30]. Here, we found a negative association of telomere length in newborn placenta with prenatal irisin. We propose more future investigations to assess the relation of pre and postnatal irisin with telomere length and telomerase activity early in human life with larger population sizes on both placenta and blood cells to provide a better answer to this question.

The third study, published in 2020, observed that irisin increases telomerase activity in aged rat hepatocytes, protecting the cells against hypoxic injury. According to this study, irisin reduced oxidative stress in the aged hepatocytes [31]. Here, in human neonates, we did not find a significant association between prenatal irisin and the placental activity of two antioxidant enzymes, GPX and SOD.

In perinatal research, the placenta is considered a significant tissue that serves as a precise 'record' of in-utero exposures [37, 38]. Additionally, it functions as a health biomarker because of its role as a master regulator of the fetal hormonal and endocrine environment [39]. Many birth outcomes have been connected to early pregnancy exposures, such as heat, pollution, and physical activity [40–43]. For some of these exposures, the association with birth outcomes was even stronger when it happened in early pregnancy compared to later [41, 42].

One of the main underlying mechanisms for these effects has been their impact on placental development and function, mediated by underlying molecular alterations in the cellular and epigenetic regulations of the placenta (DNA methylation) [37], its telomere length [18, 44], and oxidative stress resistance [45]. The telomere shortening [18, 46] and epigenetic changes [47] in the placenta act as a record of the footprints of environmental exposures from early pregnancy to birth

(environmental imprinting). A main limitation of the current study is that we have measured maternal irisin level at only one time-point during the pregnancy (the end of the first trimester). Future studies that include other time points would be beneficial in the future.

The concentration of irisin in the blood circulation increases during human pregnancy [48], but in pregnancy disorders such as preeclampsia and gestational diabetes, the circulating irisin level decreases compared to healthy people [2, 49]. Treatment of placenta samples with irisin in vitro showed that irisin activates placental adenosine monophosphate-activated protein kinase (AMPK) signaling, an important regulator of cellular energy homeostasis that is involved in trophoblast differentiation and pathology [10]. Exposure to irisin in vitro causes the differentiation and improvement of trophoblast function in cultured human placenta cells [10]. On the other hand, in a human case-control study, the relationship between irisin levels in the first trimester of pregnancy and the risk of macrosomia and placental growth factor (PIGF) levels in the mother's blood serum was seen, which is considered a negative effect for high irisin during pregnancy [4]. In this study, the high level of maternal irisin in the first trimester of pregnancy was discussed as a suggested marker for early detection of macrosomia [4]. Macrosomia is shown to be rooted in part by early placental developmental defects [50]. Therefore, the positive or negative effect of irisin on pregnancy and human placenta is still being questioned. As far as we know, no prior study has related irisin levels during pregnancy with histological and metabolic characteristics, telomere length, and antioxidant activity of the human placenta. The relation between irisin and telomere length has previously been studied only in adults [20, 30], and to the best of our knowledge, this is the first study that has assessed the connection of maternal irisin levels with the placenta developmental markers.

The three anthropometric features of the neonates' weight, height, and head circumference were assessed with a t-test, among which the neonate weight and height showed a significant association with the placental telomere length. Still, the neonates' head circumference did not show an association. Telomere length in the placenta may be considered a marker for a well-regulated development and stress response in the placenta [18, 35]. It is demonstrated that placental function is vital for fetal growth, and malfunctional placenta is one of the main factors in fetal growth restrictions such as being IUGR or having low birth weight [51]. Neonate's weight, head circumference, and height might be directly affected by the health and functionality of the placenta, as the main source of food and immunologic and endocrine exchange with the mother's body [51]. Placental telomere length has been associated with some birth and pregnancy complications, such as intrauterine growth restriction [13–18].

One of the limitations of the current study is that some factors, such as nutritional status, vitamins, and supplements [52, 53], and other factors, such as infections [54–58], and anesthetic methods [59–61] are not included in our analyses. Future larger studies are warranted to investigate the association of telomere length and irisin levels, considering the impact of the abovementioned factors.

Conclusion

We discovered an inverse correlation between prenatal irisin levels and placental RTL, but we did not find any significant link between irisin levels and the SOD and GPX enzyme activities in the term placenta. Future assessments are warranted to examine various oxidative stress markers, telomerase activity, and cellular DNA damage in the placenta regarding prenatal irisin.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13104-025-07118-1.

Supplementary Material 1

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Author contributions

F.A. performed the experiments and contributed to manuscript drafting. Z.J. contributed to the study's design, data collection, statistical analyses, and manuscript drafting; T.T., M.M., H.H., and M.R.H. contributed to the data collection and drafting of the manuscript. O.S.E. and Z.R. contributed to sample collection. P.KH. contributed to the statistical analyses; H.V. contributed to the revision of the paper; All authors read and approved the final manuscript.

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Data availability

The datasets generated and analyzed during the current study are not publicly available but are available from the corresponding author on a reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Rafsanjan University of Medical Sciences (Code of Ethics: IR.RUMS.REC.1401.105). Rafsanjan's birth cohort study registration and ethics code are 99040 (IR.RUMS.REC.1399.033). All research procedures were conducted under the supervision of the Ethics Committee of Rafsanjan University of Medical Sciences and by PERSIAN birth cohort studies guidelines and protocols. Informed consent was obtained from all participant mothers. This study was performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Disclosure statement
The authors have nothing to disclose.

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