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Research Article

The Impact of Serum and Follicular Fluid Irisin on Oocyte and Embryonic Characteristics in Infertile Women Undergoing ICSI According to BMI

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Abstract

Background: Irisin is a recently identified myokine that acts like adipokines. It has been revealed to be connected with insulin resistance (IR), obesity, and metabolic syndrome. *Objective*: To investigate serum, follicular fluid (FF), irisin, and IR in lean, overweighed, and obese women undergoing the intracytoplasmic sperm injection (ICSI) cycle and correlate them with oocyte and embryo quality. *Methods*: Ninety infertile Iraqi women aged 18 to 40 years had primary or secondary infertility. They were enrolled in this study and divided into three groups according to body mass index ranking: the first group: twenty-seven normal-weighted females, the second group: thirty-five overweighed females, and the third group: twenty-eight obese females. ICSI was done for them to evaluate the level of serum and follicular fluid Irisin with the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) at the day of oocyte pickup and correlate them to the outcome. *Results*: HOMI-IR, serum, and FF Irisin levels were significantly higher in obese people. Also, there was a significant difference between groups in regard to MII, oocyte maturity rate, grade 1 embryo, and pregnancy outcome, which was less in the obese group. In addition, there was a significant negative correlation between HOMI-IR and irisin levels in serum and follicular fluid with MII oocyte count, oocyte maturity rate, embryo grade 1, and pregnancy outcome. *Conclusion*: Serum, follicular fluid Irisin, and HOMA-IR were significantly higher in obese cases than in lean cases, which may cause a reduction in the ICSI outcome.

Keywords: Infertility, Obesity, Irisin, Intracytoplasmic sperm injection, Oocyte and embryo characteristics.

تأثير مستوى ايريسين في المصل والسائل الجريبي على البويضات والخصائص الجنينية لدى النساء العقيمات اللائي يخضعن لـ ICSI وفقا لمؤشر كتلة الجسم

الخلاصة

الخلفية: أيريسين هو ميوكين تم تحديده مؤخرا ويعمل مثل الأديبوكينات. تم الكشف عن ارتباطه بمقاومة الأنسولين والسمنة ومتلازمة التمثيل الغذائي. **الهدف**: فحص مستوى أيريسين في المصل والسائل الجريبي ومقاومة الأنسولين لدى النساء النحيفات وذوات الوزن الزائد والبدينات اللائي يخضعن لدورة حقن الحيوانات المنوية داخل الهيولى وربطها بجودة البويضة والجنين. **الطريقة**: تمت دراسة تسعون امرأة عراقية تتراوح أعمارهن بين 18 و 40 عاما مصابات بالعقم الأولي أو الثانوي. تم تقسيمهن إلى ثلاث مجموعات وفقا لترتيب مؤشر كتلة الجسم: سبع وعشرون أنثى ذات وزن طبيعي، خمسة وثلاثون أنثى مفرطة الوزن، وثمانية وعشرون أنثى بدينة. تم إجراء الحقن المجهري لهن لتقييم مستوى ايريسين في المصل والسائل الجريبي مع تقييم نموذج الاستتباب لمقاومة الأنسولين في يوم التقاط البويضة وربطها بالنتيجة. **النتائج**: كانت مستويات HOMI-IR وايريسين المصل و السائل الجريبي أعلى بشكل ملحوظ لدى الأناث ممن يعانين من السمنة المفرطة. كان هناك فرق كبير بين المجموعات فيما يتعلق بـ MII، ومعدل نضج البويضة، وجنين الدرجة 1، ونتائج الحمل، والتي كانت أقل في المجموعة البدينة. بالإضافة إلى ذلك، كان هناك ارتباط سلبي كبير بين مستويات HOMI-IR و ايريسين في المصل والسائل الجريبي وعدد البويضات MII، ومعدل نضج البويضة، ودرجة الجنين 1، ونتائج الحمل. **الأستنتاج**: كان أيريسين المصل والسائل الجريبي و HOMA-IR أعلى بشكل ملحوظ في حالات السمنة مقارنة بالحالات الخالية من الدهون، مما قد يتسبب في انخفاض في نتائج الحقن المجهري.

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INTRODUCTION

Irisin, which was first defined by Boström et al. in 2012, is a myokine that is released from the muscle after exercise, activates the Fibronectin type III domain-containing 5 (FNDC5) gene, and formats the FNDC5 protein. Irisin gets released into the bloodstream as a consequence of this protein's proteolysis. It causes the brown-fat-like conversion of white adipose tissues and is thus suggested for improving metabolic and glucose balance [1]. Since its physio-pathological value, irisin has been the topic of many investigations since its discovery. Initially, irisin was thought to be a preventive factor against diet-induced weight gain, which was caused by the browning of white adipose tissues, resulting in increased energy expenditure [2]. Adipocytes also produce irisin. The control of irisin, along with its function in glucose metabolism, is yet unclear [3]. Numerous studies have looked into the potential function of irisin in metabolic illnesses such as obesity, type 2 diabetes mellitus, nonalcoholic fatty liver disease, and cardiovascular disease, and its secretion might be augmented as a compensatory strategy in these individuals to overcome latent irisin resistance [4]. In light of these findings, we propose that irisin is a novel molecular marker and target in metabolic diseases and may have probable consequences for reproductive capability [5]. Obesity and undernutrition are both linked to reproductive dysfunction because of a strong connection between the capacity for reproduction and adipose tissue metabolism [6]. Available evidence of the vital role of biological substances including leptin, insulin, and adiponectin in reproduction is conclusive [7]. As we are all aware, obesity has become a global epidemic. It commonly coexists with metabolic and endocrine disorders and has negative effects on female fertility, pregnancy, and the health of future generations [8]. Although many studies have investigated the levels of irisin in biological fluids, its level in the follicular fluid (FF) of infertile women and its possible relationship with oocytes, embryo quality, and pregnancy outcome in different BMIs have not been reported yet. Due to the fact that oocyte and embryo quality are the keys to successful pregnancy, the aim of this study was to investigate the effects of irisin levels in serum and follicular fluid on oocyte and embryo characteristics in women undergoing the intracytoplasmic sperm injection (ICSI) cycle.

METHODS

This prospective clinical cross-sectional study involved 90 infertile females who were enrolled in assisted reproductive technology (ART) programs through ICSI. Between September 2021 and March 2023 at the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies, Al-Nahrain University. All women ranging in age from 18 to 40 years with primary or secondary infertility and various causes of infertility (tubal blockage, unovulatory cycle, unexplained infertility, and mild cases of male factor) were included. However, patients with low ovarian reserve and evidence of endocrine abnormalities, for example, thyroid dysfunction, elevated prolactin, diabetes mellitus, late-onset congenital adrenal hyperplasia, Cushing's syndrome, hypogonadotropic hypogonadism, and advanced maternal age ≥ 40 years, as well as all cases of endometriosis, except mild-type, as well as male partners with azoospermia, were excluded from the study. The sample size was calculated with this equation ($N = p \ (1-p) \ z2/me2$), where P is the prevalence rate of the infertile female (12%) according to a previous study [9]. $Z = 1.96$, $Me = 0.05$. The sample size was equal to 163. Seventy-three out of 163 female patients who were not eligible for the study were excluded (six empty follicles, twenty freezes all, six poor responses, three abnormal embryos, and three atretic embryos), and 35 refused to participate. The residual 90 infertile females were categorized into three groups according to body mass index (BMI) ranking, based on the National Institute of Health (NIH) and the World Health Organization (WHO) [10]. All couples were subjected to the basic fertility work-up of the fertility center, which includes case history, physical examination, ovulation detection, assessment of the tubal and uterine cavities, and semen analysis. BMI is calculated by measuring the female's height and weight (BMI = weight (kg)/height (m2). Controlled ovarian hyperstimulation with a flexible Gonadotropin Releasing Hormone (GnRH) antagonist regimen was used for all female participants. After oocyte retrieval, the follicular fluid was directly sent to an embryologist to gather the retrieved cumulus-oocyte complexes (COC). Following denudation, each oocyte was thoroughly examined, looking for the absence or presence of the germinal vesicle or first polar body. Oocytes that were morphologically normal and had extruded the first polar body (metaphase II) had been selected for microinjection. Intracytoplasmic sperm injection (ICSI) was done, and about 16–18 hours after ICSI, the presence of two pronuclei (2PN) and 2PB in the injected oocytes confirmed fertilization. The embryo morphology was assessed by the same embryologist, and the grading system was done according to the Istanbul consensus workshop on embryo assessment. The grading system was done based on the number of blastomeres, blastomere symmetry (equal = score 1, different = 2), and the percentage of fragmentation ($\leq 10\% =$ score 0; $11–20\% = 1$; $21–30\% = 2$; $>30\% = 3$). Under ultrasound guidance with a soft catheter, the cleavage stage (day 3) fresh embryo transfer was done [11]. luteal phase support was initiated on the day of oocyte retrieval, and beta hCG levels were measured 14 days after embryo transfer. (to document biochemical pregnancy). The measurement of irisin in serum and follicular fluid with serum insulin was done using the enzyme-linked immunosorbent assay (ELISA)

kit (Shanghai Biological, China). On the days of oocyte retrieval, each infertile woman had blood samples drawn by venipuncture. They were then centrifuged for 10 minutes at 3000 g. The serum was removed and stored at -20°C. The follicular fluid (FF) was obtained from the first retrieved follicle to avoid contamination of the blood and flushing medium and collected in a flat tube. It was frozen at -20°C for approximately 20 minutes before being analyzed. The measurement of irisin serum and follicular fluid levels was assessed by the ELISA kit. Determination of Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR) Index for the Assessment of Insulin Resistance It was first described under the name HOMA by Matthews et al. in 1985. HOMA-IR can be calculated with the following equation:

HOMA-IR = [glucose (mg/dl) × insulin (mIU/L)]/405. Normal value in adults: < 2 [12].

Ethical consideration

The study design, sample selection, and outcome evaluation are performed according to the Declaration of Helsinki and its amendments. Verbal and written consents were obtained from each participant before inclusion in the study. The Ethics Committee on Human Research of the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies, Al-Nahrain University, approved the research protocol (code 0701-PF-2021S5).

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 28.0 and Microsoft Excel 2016 were both used to code, tabulate, and statistically analyze the data. Data are presented as mean±standard deviation. The student's paired *t*-test, the Chi-square test, and the ANOVA all compared the groups. Pearson's correlation coefficient (*r*) determined the degree of association between continuous variables. The significance level was assumed to be *p*<0.05.

RESULTS

Ninety infertile females who enrolled in this study were divided into three groups according to body mass index ranking (Figure 1): first group: twenty-seven normal-weighted females second group: thirty-five overweight females, and last group: twenty-eight obese females.

Figure 1: infertile females were divided into three groups according to body mass index ranking

Table 1, Figure 2, and Figure 3 showed the main demographic information and basal hormonal profile levels (follicle-stimulating hormone, luteinizing hormone, estradiol, prolactin, and thyroid-stimulating hormone) of the patients who were studied.

Table 1: Demographic characteristics and hormonal levels of infertile women according to BMI

Characteristic	BMI 19.9-24.9 n=27	BMI 25-29.9 n=35	BMI ≥ 30 n=28	*p-value*
Age (year)	29.96±5.30	32.34±4.96	31.50±6.33	0.24
BMI (kg/m²)	23.02±0.89	26.97±1.29	32.05±1.46	<0.001
Duration of infertility (year)	4.78±3.76	5.31±2.74	5.54±3.48	0.68
AMH (pg./ml)	2.96±1.59	3.03±1.82	3.23±1.68	*0.83*
FSH (mIU/ml)	5.18±1.85	5.22±2.26	4.93±2.05	0.85
LH (mIU/ml)	5.60±1.29	5.34±1.46	5.34±2.16	0.79
Prolactin (ng/ml)	17.50±5.28	19.07±7.97	19.76±4.55	0.40
TSH (mIU/ml)	1.63±0.57	1.72±0.64	1.88±0.55	0.28
E₂(pg./ml)	35.78±8.86	37.16±7.69	35.51±8.23	0.69

Values were presented as mean±SD*; n*: number of cases; BMI: body mass index FSH: follicle stimulating hormone; LH: luteinizing hormone; TSH: thyroid stimulating hormone; E₂: estradiol.
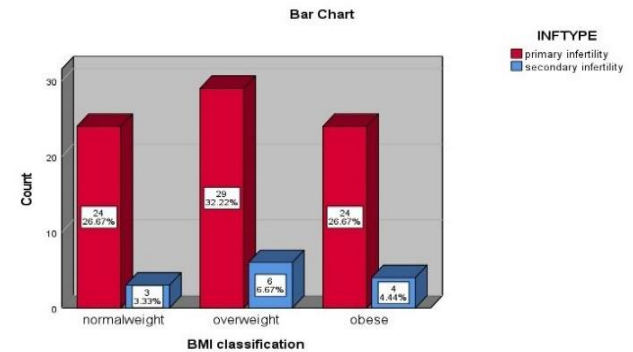

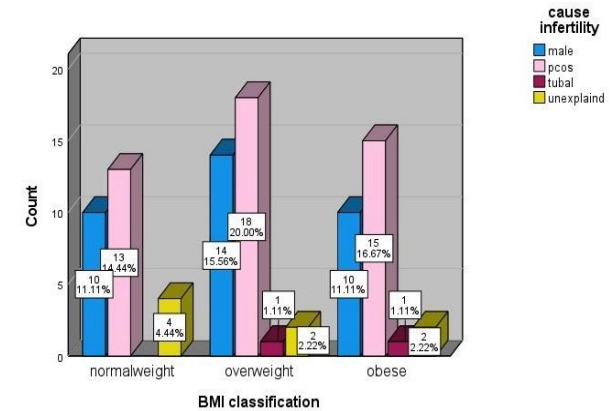**Figure 2**: The comparison between types of infertility.

Figure 3: The comparison between cause of infertility.

The statistical analysis showed no significant differences (*p*>0.05) between the groups. Table 2 illustrates significant differences between the three groups of patients regarding the total oocyte count, MII oocyte, oocyte maturation rate, and grade I embryos, which are more in the normal weight group. However, there were no significant differences regarding MI oocytes, germinal vesicles, and fertilized oocytes in grade II and grade III embryos (*p*>0.05).

Table 2: Oocyte and embryo characteristics of infertile women according to BMI

Characteristic	BMI 19.9-24.9 n=27	BMI 25-29.9 n=35	BMI ≥30 n=28	p-value
Number of oocyte	14.37±4.26	11.94±2.80	11.04±1.88	<0.001
MII oocyte	8.81±2.43	8.81±2.43	5.61±1.17	<0.001
MI oocyte	2.63±2.04	2.63±1.78	2.50±1.45	0.95
Germinal vesicle	0.96±0.58	1.09 ±0.81	1.29 ±0.60	0.22
Maturity index	65.34±15.89	57.27±11.85	52.18±14.17	0.003
Fertilized oocyte (2 PN)	73.78±17.42	65.11±18.63	64.14±18.19	0.09
Grade I	3.04±1.56	2.51±1.17	1.93±1.36	0.01
Grade II	1.15±0.90	1.31±0.86	1.71±0.93	0.6
Grade III	0.63±0.49	0.77±0.64	0.89±0.62	0.26

Values were presented as mean±SD; *n*: number of cases.

Table 3 shows that there were big differences between serum and follicular fluid Irisin and HOMA-IR. Irisin levels were highest in obese women and lowest in normal-weight women (*p*<0.001). Figure 4 demonstrated significant differences between groups regarding pregnancy rate (*p*=0.02), with the lowest pregnancy rate in obese females.

Table 3: HOMA-IR, serum Irisin and follicular fluid irisin levels of infertile women according to BMI

Characteristic	BMI 19.9-24.9 n=27	BMI 25-29.9 n=35	BMI ≥30 n=28	p-value
HOMA-IR	1.02±0.34	1.30±0.43	1.68±0.55	<0.001
Serum irisin	3.37±0.86	4.26±1.02	6.34±2.03	<0.001
Follicular Irisin	2.66±0.79	3.35±0.80	4.94±1.63	<0.001

Values were presented as mean±SD; *n*: number of cases.
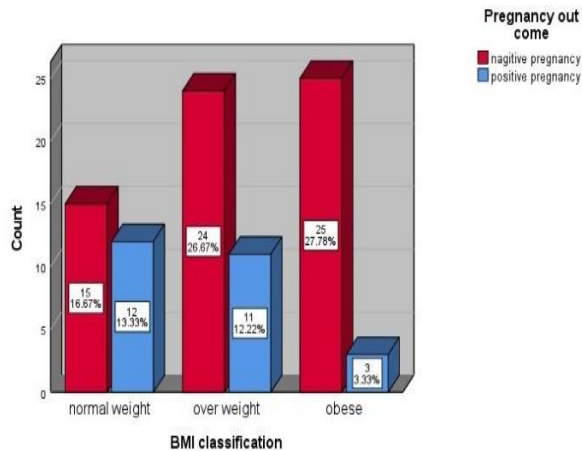

Figure 4: Pregnancy rate of patients enrolled in the current study according to BMI

Table 4 illustrates significantly lower BMI, HOMA-IR, serum, and follicular fluid Irisin levels in pregnant females when compared with non-pregnant women. Table 5 demonstrated the following significant correlations: There is a positive and significant correlation between follicular fluid irisin and serum irisin (*r*=0.902, *p*<0.001). There is a positive and significant correlation between serum and follicular fluid Irisin and HOMA-IR (*r*=0.629, *p*<0.001; *r*=0.557, *p*<0.001 respectively).

Table 4: Comparison of BMI, serum and follicular fluid irisin levels, and HOMA-IR between pregnant and-non pregnant females

Parameter	Pregnant n=26	Non-Pregnant n=64	p-value
BMI	25.45±3.08	28.14±3.76	0.002
Serum irisin	3.52±0.63	5.10±1.95	<0.001
Follicular fluid Irisin	2.68 ±0.46	4.03±1.53	<0.001
HOMA-IR	1.02±0.24	1.46±0.54	<0.001

Values were presented as mean±SD; *n*: number of cases.

Positively significant correlation between serum, follicular fluid irisin, and HOMA-IR with BMI (*r*=0.627, *p*<0.001; *r*=0.628, *p*<0.001; *r*=0.376, *p*<0.001, respectively). There is a significant negative correlation between HOMA-IR, serum, and follicular fluid Irisin with metaphase II oocytes (*r*=0.316, *p*<0.001, *r*=0.344; *p*<0.001 *r*=0.353, *p*<0.001, respectively). There is also a significant negative correlation between HOMA-IR, serum, and follicular fluid Irisin and maturation rate (*r*=0.543, *p*<0.001; *r*=0.396, *p*<0.001, *r* =0. 324, *p*<0.001, respectively). A negative and significant correlation was reported between Grade 1 embryos with HOMA-IR, serum, and follicular fluid irisin (*r*=0.402, *p*<0.001; *r*=0.281, *p*<0.001; *r*=0.289, *p*<0.001, respectively). A negative and significant correlation was reported between pregnancy outcome and HOMA-IR, serum, and follicular fluid irisin (*r*=0.351, *p*<0.001; *r*=0.402, *p*<0.001; *r*=0.431, *p*<0.001, respectively). Additionally, a negative and significant correlation was detected between fertilized oocytes and follicular fluid Irisin (*r*=0.250, *p*<0.05). A positive and significant correlation was reported between Grade 11 embryos and serum irisin (*r*=0.262, *p*<0.001).

Table 5: Correlations between HOMA-IR, serum and follicular fluid irisin with ICSI outcome

Parameters		HOMA-IR	S. irisin	F.F irisin
F.F irisin	r	0.557*	0.902*	-----
HOMA-IR	r	-----	0.629*	0.557*
BMI	r	0.376*	0.627*	0.628*
Total oocytes count	r	0.102	-0.070	-0.137
Metaphase II oocytes	r	-0.316*	-0.344*	-0.353*
Metaphase I oocytes	r	0.276	0.110	0.032
GV	r	0.175	0.184	0.134
Maturation rate	r	-0.543*	-0.396*	-0.324*
Fertilization rate	r	-0.172	-0.180	-0.250*
Grade 1 embryos	r	-0.402*	-0.281*	-0.289*
Grade 2 embryos	r	0.165	0.262*	0.206
Grade 3 embryos	r	0.143	0.159	0.071
pregnancy	r	-0.351*	-0.402*	-0.431*

*: Significant correlation; *r*: Pearson's correlation coefficient.

DISCUSSION

The current study looked at the levels of irisin in the blood and follicular fluid of infertile women with different BMIs who had ICSI therapy for insulin sensitivity. The study also looked at how well the ICSI therapy worked for these women. Based on what is known and what can be found in scientific papers, this

is the first study to look at serum and follicular fluid levels of irisin with IR in different groups of women going through ICSI cycles based on their BMI and ICSI outcomes. This study shows that serum and follicular fluid levels of irisin were significantly higher in obese women compared to overweight or normal BMI women. With high IR and a lower ICSI outcome in this study, a significant percentage of enrolled infertile females are either overweight or obese, as they are in combination, about 63%. This observation can be explained in two ways: The first one is that being overweight or obese is common in our community, according to statistics from numerous Iraqi studies [13]. The second possibility is a link between high BMI (overweight and obesity) and female infertility [14]. In the present study, there were more oocytes retrieved, metaphase II oocytes (mature oocytes), and maturity index in the normal weight group than in the overweight and obese groups. These results are supported by some studies that found obese women had lower oocyte retrievals and lower-quality oocytes than women of normal weight [8,15]. And also, these findings are in line with other research that suggests obesity may provide a risk for adverse IVF outcomes, such as unsuccessful fertilization, pregnancy, increased miscarriage, and cycle cancellation [18–16]. The statistical analysis showed that there was a significant difference in the percentage of good-quality embryos (GI) in the normal-weight ICSI group, while there was no significant difference in the percentage of embryos in grades II (GII) or III (GIII). These findings support previous research showing that obese women are more likely to produce poor-quality embryos [8,19,20]. The present work is an attempt to explore the effect of irisin on follicle development by measuring FF and serum levels of these molecules in patients that reveal a negative correlation with metaphase II oocytes, maturation rate, and Grade 1 embryos. Adipose tissue, a female's energy storage reserve, is necessary for the start and continuation of reproductive processes. Disturbance in the adipose mass has a deleterious impact on female fertility [21]. Irisin causes various adipose tissue reactions that raise the body's overall energy expenditure by promoting browning and Uncoupling Protein 1 (UCP1) expression [5]. Irisin may help follicle development by controlling the changes in temperature inside follicle cells [3]. Thus, high amounts of FF-Irisin may impair the capacity of infertile women's oocytes and follicle cells to use energy. As a result, uneven serum and FF-Irisin levels can lead to inappropriate follicle development [22,23]. Furthermore, during follicular development, irisin resistance in follicle cells might affect angiogenesis and mitochondrial biogenesis. According to previous research, irisin affects oxidative metabolism and mitochondrial biogenesis in a variety of cell types [24]. The HOMA-IR is a simple, quick, and painless way to assess insulin resistance and a non-invasive method to measure insulin resistance [25]. Insulin resistance (IR), which rises with increasing body weight, these findings agreed with other earlier research [23,26–27]. In the present study, serum and FF Irisin levels are positively correlated with markers of insulin resistance (such as HOMA-IR and BMI) in the overall patient population, in agreement with previously available work. The first study to show that serum irisin levels in humans were positively correlated with IR and obesity was published by Moreno-Navarrete and colleagues [28]. Also, Tang et al. and Mai et al. stated a positive correlation between circulating Irisin and HOMA-IR [29,30]. Patients with type-2 diabetes mellitus or gestational diabetes mellitus (GDM) have impaired irisin metabolism [31]. Irisin is currently thought of as an adipo-myokine, as adipose tissue, a target for Irisin, may also release this hormone [32,33]. It was proposed that normal ovarian physiology is maintained by interactions between the endocrine components of muscle, adipose tissue, and ovarian tissues [34]. In this study, the FF and serum Irisin levels were significantly higher in obese and overweight people as compared with normal weight [$P \le 0.001$], and these changes are associated with insulin resistance (high HOMA-IR), which may represent a way to counterbalance the higher Irisin requirements; or due to an underlying decreased sensitivity to Irisin's effects (Irisin resistance), which results in a compensatory increase in Irisin levels; or because of increased Irisin secretion by the increased muscle and fat tissue in obesity, high circulating Irisin levels and insulin resistance in obesity can be explained [35]. In the present study, there was a significant correlation between irisin levels and BMI. Some studies observed a positive correlation of irisin levels with BMI [36–39], while no correlation was reported by Gonzalez-Gil et al. [40]. This discrepancy across research may be caused by myocytes and/or adipose tissue expressing irisin in unknown situations. The prevalence of variation in the proportion of women with increased body weight among patients around the world and variations in the distribution of abdominal or visceral adiposity are linked to variations in insulin resistance that can affect metabolic and reproductive function, discrepancies in laboratory measures, ethnic heterogeneity, genetic background, level of physical activity, etc. Irisin detection methods, kits, and the heterogeneity of patients with metabolic abnormalities included in each study are likely to be responsible for the controversial results regarding Irisin levels [41]. The results of the present study showed that in regard to the pregnancy rate according to body mass index ranking, there were significant differences between groups. The lower pregnancy rate was found in obese females (3.33%). Also, the results showed a significantly lower BMI in pregnant females. Obesity has a marked effect on fertility, which is frequently accompanied by metabolic and endocrine disorders. Obese women are more likely to have reproductive issues such as infertility, difficulties in embryonic development, and abnormal

offspring [7]. The effects of female obesity on the emergence of various reproductive problems are mediated by a variety of pathways, making female obesity a complicated multifactorial syndrome. Hyperinsulinemia, insulin resistance, hyperandrogenism, lipotoxicity, and inflammation are the chief mechanisms [42]. Yet, the exact mechanism regarding their correlation is still uncertain. This outcome was consistent with other findings that indicated a detrimental impact of obesity on rates of conception [8,43]. In the results of the present study, there were significantly lower serum and follicular fluids. Irisin levels in pregnant females, and a negative correlation was found between serum and FF Irisin levels and pregnancy outcome in all women enrolled in the study. Attempting to evaluate the possible impact Irisin might have exerted on non-adipose tissues such as the follicle can be challenging. Irisin, regardless of the underlying causes of infertility, may aid follicle and oocyte development and function by preserving local thermoregulation [44]. It may be clarifying the above result that inappropriate serum and FF irisin levels affect oocyte function and development, which contribute to pregnancy outcomes. The authors are aware of the small sample size due to different factors. One is that cultural beliefs limit the response rate. Second, a probability of sampling bias is not uncommon because there is no documented data related to the size of the required population.

Conclusion

Serum, follicular fluid Irisin, and HOMA-IR were all much higher in obese people than in thin people. This may cause a drop in the number of oocytes, the quality of embryos, and the chance of getting pregnant. Obesity in women carries the risk of infertility and negative effects on the fetus and offspring. Fortunately, these adverse outcomes can be avoided by moderate weight loss. Meanwhile, for the health of more women, more research is needed to further understand the relationship between obesity and female reproduction.

Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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