

Metabolic Syndrome and Assisted Reproductive Techniques

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Abstract

Objective: Metabolic syndrome is a risk factor affecting reproductive health and pregnant outcomes. So far, the effect of this syndrome on the success rate of assisted reproduction techniques (ART) has not been investigated. The aim of this study was to investigate the relationship between metabolic syndrome and the success rate of ART in infertile women in Isfahan.

Materials and methods: A prospective cohort study performed on 147 women candidates using in-vitro fertilization/ intra cytoplasmic sperm injection (IVF/ICSI) and/or ICSI methods referred to Isfahan Infertility Center in two groups with metabolic syndrome(n=49) without metabolic syndrome(n=98), by convenience sampling methods in Isfahan, Iran in 2018. Body mass index (BMI) and waist, abdominal circumference, Serum triglyceride (TG), cholesterol and FBS were measured. If β HCG test was positive (day 15-16 after ART), transvaginal sonography (TVS) was done 15 days later. Pregnant women were followed up to the 20th week of pregnancy. To analyze, t-test, chi-square and logistic regression tests were used.

Results: The frequency of metabolic syndrome was 33.4% (n=49).The frequency of ART was not significantly different between women with and without metabolic syndrome ($p=0.321$). The relative frequency of pregnancy ($p=0.907$) and abortion ($p=0.896$) did not show a significant difference between the two groups. Independent t-test showed that the mean FBS, HDL, TG, systolic and diastolic BP, abdominal circumference and BMI in the studied units did not differ significantly based on the occurrence of pregnancy and abortion.

Conclusion: According to the results of this study, there was no significant difference between the indicators of metabolic syndrome and the success rate of ART in achieving, pregnancy and pregnant outcomes in the first twenty weeks of pregnancy.

Keywords: Infertility; Metabolic Syndrome; Assisted Reproductive Technique; Body Mass Index; Iran

Introduction

Metabolic Syndrome can be identified by the

following criteria: abdominal obesity, insulin resistance, impaired glucose metabolism, hypertension and dyslipidemia. The health consequences associated with metabolic syndrome increase the risk of endometrial cancer, polycystic

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ovary syndrome, heart disease, obesity, and diabetes. The increasing prevalence of obesity has been significant worldwide (1). The results of the study show that obesity, followed by metabolic syndrome, affects more than 20% of American women of childbearing age (2). Unfortunately, the prevalence of metabolic syndrome in infertile couples is 10 times higher than the general population (3).

Studies have shown a high prevalence of metabolic syndrome in infertile women with polycystic ovary syndrome (4). Polycystic ovary syndrome (PCOS) affects about 13-18% of all women of childbearing age. Lack of ovulation, hyperandrogenism, polycystic ovaries, hyperinsulinemia, hirsutism and increased LH concentration are the most important consequences of PCOS. Lack of ovulation is one of the underlying causes of infertility and therefore requires the use of assisted reproductive techniques (5, 6).

Metabolic syndrome also affects reproductive health and pregnancy, so people with this syndrome are at increased risk of menstrual disorders, infertility and miscarriage (7, 8). A number of studies have shown no significant relationship between infertility and cardiovascular disorder and metabolic syndrome (9), while another group of studies has shown a link between polycystic ovary syndrome in infertile couples and metabolic syndrome (10, 1).

Infertility is a common problem all over the world today. Studies have estimated the prevalence of infertility to be around 18-9%. Therefore, increasing the prevalence of infertility in this group will expose them to the use of assisted reproductive technologies (11). The success rate of assisted reproductive techniques in people with this syndrome is an important issue for which there is consensus among various studies. The results of a retrospective cohort study in 2011 by Luke et al. showed that the incidence of ovulation disorders and uterine tube disorders increases with increasing BMI. Increased BMI is significantly associated with decreased FSH levels and increased doses of clomiphene to stimulate ovulation in infertile women, which in turn reduces unstimulated cycles (12). While the results of a retrospective study by Sathya et al. In 2010, after IVF and ICSI, showed that there was no relationship between increased BMI and decreased number and quality of oocytes, fertilization, pregnancy rate, number of quality embryos (13). While Broughton and Moley study in 2017 showed that obesity and metabolic syndrome, even with regular menstrual

cycles, reduce the rate of pregnancy and the success of in vitro fertilization (IVF) (2). Therefore, due to the higher prevalence of metabolic syndrome in infertile women and the existence of inconsistencies in the findings, the aim of this study was to investigate the relationship between metabolic syndrome and the success rate of assisted reproductive techniques in infertile women in Isfahan.

Materials and methods

The present study was a prospective cohort study on 147 infertile couples referred to the Isfahan Fertility and Infertility Center. That which was carried out from January 2017 to June 2018.

In this study, a total of 149 infertile women who were candidates for assisted reproductive techniques were included in the study. Due to the impossibility of following up, 2 of them were excluded from the study. Data was collected and analyzed from 147 infertile women.

Inclusion criteria included: being Iranian, age 18-40 years, infertility due to female cause, spouse not having infertility, inclusion in the list of assisted reproductive Technique (ART): IUI, IVF, ICSI. Exclusion criteria also included: unwillingness to participate, failure to follow treatment instructions during the study.

Sampling was performed convenience method among women who met the above inclusion criteria. Research units based on metabolic syndrome criteria were divided into two groups of exposure (with metabolic syndrome) and non-exposed group (without metabolic syndrome).

The researcher referred to the Infertility Reproduction Center every day from 8:00 AM to 2:00 PM and in the doctor's room at the last visit before performing assisted reproductive procedures and based on the entry and exit criteria, qualified people participated in the study and after Expression of study Objectives in case of agreement to participate in the study, a written informed consent was obtained. First, the demographic characteristics of the samples (age, education, female occupation, type of infertility, cause of infertility, previous pregnancy history) were recorded in a questionnaire. Then, HDL, triglyceride, fasting blood sugar test application form was delivered to the research units.

They were asked to go to the laboratory (Erythron) for tests. During the assisted reproduction procedure, first the test results were recorded in a checklist, then height and weight, abdominal circumference and blood

pressure of women were measured, BMI was calculated and recorded in a checklist. BHCG test was requested on days 15-16 after assisted reproductive procedures, and if the test was positive, vaginal ultrasound was requested 15 days later. Pregnant women were followed up to the 20th week of pregnancy for continued pregnancy or abortion.

Data entry was performed using SPSS IBM (version 19). Results were reported as mean, standard deviation, frequency and percentage. To analyze the results, t-test, chi-square and logistic regression tests were used. Significance level P was considered less than 5.

Results

The results of the present study on 147 pregnant women candidates for assisted reproductive techniques showed that the mean and standard deviation of age of women in the group with metabolic syndrome and no syndrome were 33.8 ± 5.73 and 31.4 ± 4.91 , respectively. The mean and standard deviation of age of spouses in the affected and non-affected groups were 37.8 ± 5.74 and 36.8 ± 6.21 , respectively. Independent t-test showed that the mean age of women with and without metabolic syndrome was significantly different ($p = 0.009$) but the mean age of their husbands was not significantly different between the two groups ($p = 0.352$). Chi-square test also showed that the type of occupation of the study units ($p = 0.119$) and their spouses ($p = 0.814$) were not significantly different between the two groups. More than two-thirds of women in both groups were housewives and more than half of their husbands were self-employed.

The frequency of metabolic syndrome in the studied units was 33.4% (49 women). Chi-square test showed that there was no significant difference between the frequency of the type of ART ($p = 0.321$). Also, the frequency of abortions among the studied units was estimated to be 27.2% (40 people). Therefore, 50.6% of pregnancies (79 cases) resulted in abortion. Out of 49 women with metabolic syndrome, 26 became pregnant, of which 13 (50%) had abortions. In the group of women without this syndrome, 53 people became pregnant, of which 27 pregnancies (50.9%) led to abortion. Therefore, the relative frequency of pregnancy ($p = 0.907$) and abortion ($p = 0.896$) did not show a significant difference between the two groups.

Results of this study showed that relative frequency of pregnancy in the two groups did not have significant differences of each other ($p = 0.907$). Independent t-test showed that the mean FBS, HDL, TG, systolic and diastolic blood pressure, abdominal circumference and BMI in the studied units did not differ significantly based on the occurrence of pregnancy and abortion ($p > 0.05$) (Table 1).

Chi-square test showed that the relative frequency of pregnancy based on age groups less than and more than 35 years in the studied units did not differ significantly ($p = 0.47$) (Table 2).

The results showed that the incidence of abortion was not significantly different between the two groups ($p = 0.896$). According to Chi-square test, the relative frequency of abortions according to the indicators of metabolic syndrome was not significant ($p > 0.05$) (Table 3).

Table 1: Comparison of the relative frequency of metabolic syndrome indices in the studied units based on the occurrence of pregnancy

Metabolic syndrome index	Pregnancy status		Chi-square test		
	Occurrence of pregnancy n (%)	Absence of pregnancy n (%)	χ^2	P	
TG	≤ 150	63(53.8)	54(46.2)	0.003	0.960
	> 150	16(53.3)	14(46.6)		
HDL	> 50	14(40)	21(60)	3.489	0.062
	≤ 50	65(58)	47(42)		
FBS	≤ 110	70(52.2)	64(47.8)	1.376	0.241
	> 110	9(69.2)	4(30.8)		
BP	$< 130/85$	68(55.7)	54(44.3)	0.868	0.352
	$\geq 130/85$	11(44)	14(56)		
Waist	< 89 cm	20(46.5)	23(53.5)	1.278	0.258
	≥ 89 cm	59(56.7)	45(43.3)		
BMI	< 25	26(42)	36(58)	6.616	0.067
	25-29.9	30(63.8)	17(36.2)		
	≥ 30	23(60.5)	15(39.5)		

Table 2: Comparison of the relative frequency of pregnancies by age groups less than and over 35 years in the studied units

Variable	Pregnancy status		Chi-square test		
	Occurrence of pregnancy n (%)	Absence of pregnancy n (%)	χ^2	P	
Age	Age \geq 35 years	58(73.4)	54(79.4)	0.51	0.47
	Age <35 years	21(26.6)	14(20.1)		
Total		79(100)	68(100)		

Discussion

The results of the present study showed that only one third of the study population had metabolic syndrome. The results also showed that having metabolic syndrome does not affect the success rate of achieving pregnancy. Metabolic syndrome and BMI had no effect on pregnancy outcomes resulting from assisted reproductive techniques in the first 20 weeks of pregnancy, including abortion. While the results of the cohort study in 2020 on 3079 patients showed that the live birth rate in low weight and normal weight patients with PCOS under IVF with freeze-all strategy was the highest while there was a gradual and significant decrease in live birth rate and increased abortion rate in obese patients with PCOS (14).

Also, in a cohort study of 239,127 IVF cycles performed solely due to PCOS or male-induced infertility (proper control of other confounding variables in the success of the ART) between 2010-2010, the success rate of the ART in those with thin and normal BMI was more. While the rate of failure of the method and other complications of pregnancy in women with obese BMI and overweight was significantly increased (15). It is important to note that a study of 10,287 IVF / ICSI cycles in 2020 showed that performing surgeries such as bariatrics

and significant weight loss following surgery did not improve the prognosis and results of ART such as IVF (16). Therefore, significant weight loss through surgery for infertile women with obesity has not had a significant effect on the prognosis of IVF.

Although the results of the present study showed that there is no significant difference in the incidence of abortion between people with and without metabolic syndrome, Broughton and Moley study in 2017 showed that having metabolic syndrome due to inflammatory changes and cell damage leads to placental abnormalities. This has led to an increased incidence of miscarriage, stillbirth and preeclampsia in these women (2).

Also, contrary to the present study, Luke's 2017 study showed that having metabolic syndrome during the reproductive years is associated with adverse health consequences such as increased infertility, miscarriage, stillbirth, congenital anomalies and pregnancy complications. The results also showed that women with metabolic syndrome, especially obesity, had a reduced IVF success rate, needed higher doses of gonadotropins, a reduced risk of live birth, and risk of miscarriage and pregnancy complications such as preeclampsia and preterm labor are higher in them.

Table 3: Comparison of the relative frequency of metabolic syndrome indices in the studied units based on the occurrence of abortion

Metabolic syndrome index	Pregnancy status		Chi-square test		
	Occurrence of Abortion n (%)	Absence of Abortion n (%)	χ^2	P	
TG	\leq 150	31(26.9)	86(73.5)	0.148	0.7
	$>$ 150	9(30)	21(70)		
HDL	$>$ 50	7(20)	28(80)	1.206	0.272
	\leq 50	33(29.4)	79(70.6)		
FBS	\leq 110	36(26.2)	98(73.1)	0.091	0.763
	$>$ 110	4(30.7)	9(69.3)		
BP	$<$ 130/85	35(28.7)	87(71.3)	0.657	0.418
	\geq 130/85	5(20)	20(80)		
Waist	$<$ 89 cm	11(25.6)	32(74.4)	0.081	0.775
	\geq 89 cm	29(27.8)	75(72.2)		
BMI	$<$ 25	14(22.5)	48(77.5)	3.100	0.212
	25-29.9	17(36.1)	30(63.9)		
	\geq 30	9(23.7)	29(76.3)		

However, the results of the study showed that racial and ethnic differences in the incidence of overweight and obesity affect the results of IVF. Therefore, the results of a study showed that the probability of IVF failure in Asian women with normal and obese weight is higher (17). Contrary to the results of our study, Chenggang et al. study in 2019 represented metabolic syndrome affects the quality and number of eggs and embryos due to functional changes in the hypothalamic-pituitary-ovarian axis. Due to its harmful effect on the endometrium for accepting pregnancy, this syndrome also reduces the chances of successful ART and increases the risk of miscarriage and other adverse pregnancy outcomes (18).

Similar to the present study, the results of studies conducted by Sathya 2010, Vilarino 2011 showed a lack of correlation between the success of assisted reproductive techniques and high BMI (13, 19). The semen quality and obesity in men, which affects the quality of fetus, were studied neither in our study, nor in those two other studies.

The results of a study by Friedler et al. in 2017 on 1654 ICSI cycles was similar to our study. They showed although the number of previous ART cycles was lower in women with normal body mass index, BMI did not affect the results of assisted reproductive techniques (20). Our study did not show a significant relationship between metabolic syndrome, overweight and obesity, and having a waist size greater than 89 with the success rate of assisted reproductive techniques. However, many studies have shown the negative impact of metabolic syndrome on oocyte potential for fertilization. These variables seem to affect the quality of the egg and blastocyst more than they affect the success of the ART. Women who entered our study were those who had reached the pickup stage. In fact, it is possible that metabolic syndrome affected the development of oocytes that were not included in our study. Therefore, women with this syndrome, if they can produce eggs with the appropriate potential to stimulate ovulation, after fertilization and embryo transfer, they will be in the same conditions as others for pregnancy and the continuation of pregnancy.

It is important to note that infertility is often associated with other medical disorders, so it is difficult and seemingly inaccessible to differentiate between the effects of conditions such as metabolic syndrome on the results of assisted reproductive techniques (9). The small sample size of women

entering all causes of infertility was one of the limitations of the present study.

Conclusion

According to the results of this study, there was no significant difference between the indicators of metabolic syndrome and the success rate of ART in achieving pregnancy and pregnancy outcome in the first twenty weeks of pregnancy.

Conflict of Interests

Authors declare no conflict of interests.

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