Body Mass Index, Follicle-Stimulating Hormone and their Predictive Value *in vitro* Fertilization

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The aim of this study was to determine if body mass can be considered a risk factor for infertility, and if we can find any correlations between the age values and the FSH and estradiol values, and between the BMI values and the FSH and estradiol values. Our whole sample contains 100 patients splinted in two groups (pregnant patients N1=57 subjects, 57%, and not – pregnant patients N1=43 subjects,43%). In the first part we conducted our analysis on the whole group and after that we focused the analysis on the two groups and we made some comparisons between the groups. We obtained a medium, extremely significant correlation in all scenarios between the age and the FSH values. This is the best association from all the cases which we tested. In all twelve cases we have a positive correlation (r > 0). As well, we obtained that a BMI value higher than 25can be considered a risk factor for obtaining a pregnancy (p<0.05, RR > 1, OR>1) . Our study shows that women who have weight problems have much less chances of conceiving a baby, even if they ovulate normally. The risk of infertility increases proportionally to the extra pounds. Irregular ovulation in women is the most common fertility disorder due to obesity disease.

Key words: body mass index, follicle-stimulating hormone, estradiol, vitro fertilization, pregnancy

A large number of suraponderal women suffer from infertility. A high percentage of infertile patients are diagnosed with polycystic ovary syndrome, a commonly associated disorder with obesity, chronic anovulation and irregular menstruation to which hyperandrogenism and hyperinsulinaemia are added (or not). Anovulation also occurs in female patients with IMC>30 because of abnormal secretion of hormones GnRH (hormone-releasing gonadotropin), LH (hormonal luteinizing) and FSH (folliculo stimulant hormone)[1-3]. Obesity is an epidemic affecting millions of women around the world, and one in four women is at least overweight, according to a study. The disorder also has a negative effect on the ability of a woman to carry a pregnancy term safely. Together with other sexual health issues, infertility is one of the consequences of obesity [4].

According to studies, overweight or obese women show a 30% higher risk of developing infertility due to anovulation. Those with an IMC greater than 31 exhibit a 170% higher risk of infertility. If at least 5% of excess adipose tissue is eliminated, the ovulation rate may increase and biochemical abnormalities will also be reduced.

Studies have shown that for women suffering from obesity and also anovulation, the most likely cause of obesity is polycystic ovary syndrome. It is associated with obesity or overweight and with the symptoms of too abundant secretion of male hormones such as excess hair loss, acne, high cholesterol and insulin resistance [5-8].

Categories of BMI: We used the classification of BMI recommended by the World Health Organization (WHO) and the Centers for Disease Control for *overweight* (25–29.9), *obese* (30–34.9) and *severely obese* (≥35). We categorized men with BMI <20 as *underweight* (comprising 1% of our sample), and *a priori* we selected *low normal* BMI (20–22.4) as the referent in analyses. Since our sample size was large, we split each of the broad WHO categories of normal, overweight and obese into a total of eight BMI categories (<20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, 30.0–32.4, 32.5–34.9 and 35+) [3] .

Experimental part

Material and method

The 100 patients were taken from the database of the County Emergency Clinical Hospital, Timisoara - Bega Gynecology Obstetrics Section. The data were collected between 2015 and 2017, the design of the study is a follow up study. The main idea of the study was to see if a higher body mass index (IBM) can influence the process of fertility. Anamnestic, the patients in the study have a regular menstrual cycle. For all the subject we collected their age, if they are smokers or non - smokers, their height and weight in order to calculate the BMI. As well, we ran some tests in order to determine the FSH and estradiol values. We analyzed two different cases: when we look at the group as a whole and the second scenario is when we split the

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group in two: the group of pregnant patients (N1=57 subjects, 57%) and the group of patients who are not pregnant (N2=43 subjects, 43%).

Statistical analysis

The database of 100 patients was created using the Microsoft Excel software. The statistical calculations were performed using SPSSv17, EpiInfo and Microsoft Excel.

Results and discussions

For a better view of our database we computed some descriptive statistics on the numerical variables. The patients of our study have the age between 22 and 40 years. The mean value of the sample is 32 and the mode value is 37. If we divide the sample in two regarding the pregnancy test we can say that the first group (N1=57), where the patients are pregnant is younger than the second group (N2=43). The mean value in the first group is 31 years and in the second group is 33 years, but the differences are not statistically significant ($p=0.09$). For determining the significance of the differences we applied a Man – Whitney test. All the statistical data are presented in tables 1,2 and 3.

Further-on, we tested to see if there is any association between the age values and the FSH and estradiol values, and between the BMI values and the FSH and estradiol values. For this we calculated the Pearson coefficient (r) and the determination coefficient [(R^2)]and in order to see if the association between the variables is significant we applied a regression model. We presented three different scenarios: first case when we analyze the whole sample, second case when we analyze only the pregnant patients and the last case when we take in consideration only the patients who are not pregnant (table 4, 5 and 6). We plotted the most significant case of correlation (fig.1). We can say that we have a medium, extremely significant correlation in all three scenarios between the age and the FSH values. This is the best association from all the cases which we tested. In all twelve cases we have a positive correlation ($r>0$), and the cases in which the association is statistically significant we underlined them with grey (table 4-6).

Statistics / Variables, N=100	Age	BMI	FSH	Estradiol
Mean	32	25.11	6.916	24.28
Standard Error	0.46	0.15	0.12	0.50
Median	32	25	6.9	24
Mode	37	24	7.1	27
Standard Deviation	4.59	1.53	1.18	5.01
Sample Variance	21.06	2.34	1.40	25.13
Range	18	8	5.9	20
Minimum	22	22	3.9	14
Maximum	40	30	9.8	34
Count	100	100	100	100

Table 1
DESCRIPTIVE STATISTICS FOR THE WHOLE SAMPLE (N=100)

Statistics / Variables, N1=57	Age	BMI	FSH	Estradiol
Mean	31	24.84	6.67	24.51
Standard Error	0.57	0.18	0.15	0.58
Median	31	25	6.3	25
Mode	31	24	5.7	21
Standard Deviation	4.28	1.35	1.16	4.41
Sample Variance	18.29	1.81	1.34	19.47
Range	17	7	5.8	16
Minimum	22	22	3.9	16
Maximum	39	29	9.7	32
Count	57	57	57	57

Table 2
DESCRIPTIVE STATISTICS FOR THE GROUP WHO TESTED POSITIVE AT THE PREGNANCY TEST (N1=57)

Statistics / Variables, N2=43	Age	BMI	FSH	Estradiol
Mean	33	25.47	7.24	23.98
Standard Error	0.74	0.26	0.18	0.88
Median	35	26	7.1	24
Mode	36	26	7.1	19
Standard Deviation	4.87	1.70	1.15	5.75
Sample Variance	23.72	2.87	1.33	33.12
Range	18	8	5.1	20
Minimum	22	22	4.7	14
Maximum	40	30	9.8	34
Count	43	43	43	43

Table 3
DESCRIPTIVE STATISTICS FOR THE GROUP WHO TESTED NEGATIVE AT THE PREGNANCY TEST (N2=43)

Table 4

THE ASSOCIATION BETWEEN THE AGE VARIABLE AND THE FSH AND ESTRADIOL VALUES, AND BETWEEN BMI AND FSH, RESPECTIVELY BETWEEN BMI AND ESTRADIOL FOR THE WHOLE SAMPLE

For the whole sample N=100	*Correlation between*			
Statistics / Variables	Age and FSH	Age and Estradiol	BMI and FSH	BMI and Estradiol
Pearson coefficient (r)	0.44	0.32	0.21	0.19
Determination coefficient R^2	0.19	0.10	0.04	0.04
p – value obtained from the regression model	p<0,000	p=0.001	p=0.039	p=0.05

Table 5

THE ASSOCIATION BETWEEN THE AGE VARIABLE AND THE FSH AND ESTRADIOL VALUES, AND BETWEEN BMI AND FSH, RESPECTIVELY BETWEEN BMI AND ESTRADIOL FOR THE PATIENTS WHO TESTED POSITIVE AT THE PREGNANCY TEST

For the whole sample N1=57	*Correlation between*			
Statistics / Variables	Age and FSH	Age and FSH	Age and FSH	Age and FSH
Pearson coefficient (r)	0.45	0.27	0.28	0.25
Determination coefficient R^2	0.20	0.07	0.08	0.06
p – value obtained from the regression model	p=0.0004	p=0.04	p=0.03	p=0.06

Table 6

THE ASSOCIATION BETWEEN THE AGE VARIABLE AND THE FSH AND ESTRADIOL VALUES, AND BETWEEN BMI AND FSH, RESPECTIVELY BETWEEN BMI AND ESTRADIOL FOR THE PATIENTS WHO TESTED NEGATIVE AT THE PREGNANCY TEST

For the whole sample N1=57	*Correlation between*			
Statistics / Variables	Age and FSH	Age and FSH	Age and FSH	Age and FSH
Pearson coefficient (r)	0.38	0.37	0.05	0.13
Determination coefficient R^2	0.14	0.13	0.00	0.02
p – value obtained from the regression model	p=0.01	p=0.02	p=0.77	p=0.39

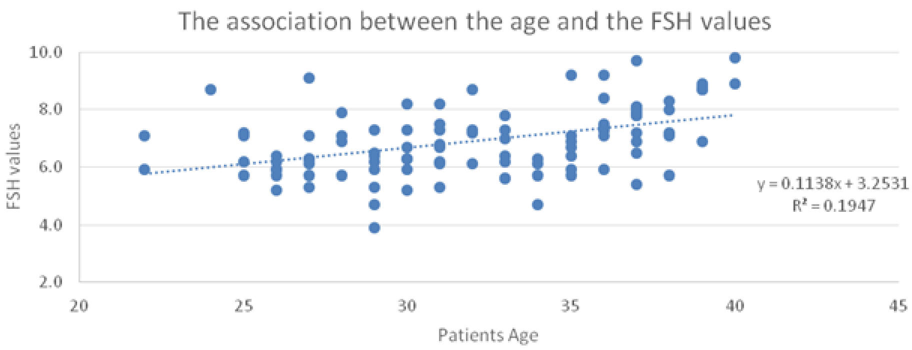

Fig. 1 The association between the age and the FSH values for the whole sample

Table 7

THE RISK ANALYSIS FOR THE WHOLE SAMPLE (N=100). IF RR,OR > 1 WE CAN SAY THAT A BMI > 25 CAN BE CONSIDERED A RISK FACTOR FOR FERTILITY. BECAUSE THE P VALUE FOR OUR TEST IS LOWER THAN OUR THRESHOLD VALUE (P=0.02 < 0.05) WE WILL SAY THAT THE RISK OBSERVED IN OUR SAMPLE CAN BE CONSIDERED SIGNIFICANT FOR THE WHOLE POPULATION.

	Negative pregnancy test	**Positive pregnancy test**	**Total**	**Statistical results**
BMI>25	22	16	38	$p = 0{,}02$ $RR = 1{,}7\ ; 95\% \in (1{,}09\ ;\ 2{,}66)$ $OR = 2{,}68\ , 95\% \in (1{,}17\ ; 6{,}17)$
BMI<=25	21	41	62	
Total	43	57	100	

In the last part we ran a risk analysis in order to see if a high BMI can induce infertility. Usually, a high BMI can produce other medical disorders, as cardiovascular disease [9-13] hematological disease [14-17], or kidney failure [18].

We considered as a risk factor a BMI value higher than 25. Our study is a protective study, so we calculated the relative risk (RR) and the odds ratio (OR) for our sample (N=100). We obtained that a BMI value higher than 25 decreases significantly (p<0.05) the chances of a future pregnancy. To determine the significance of our differences we applied a χ^2 test for proportions. All the data is presented in table 7 and plotted in figure 2.

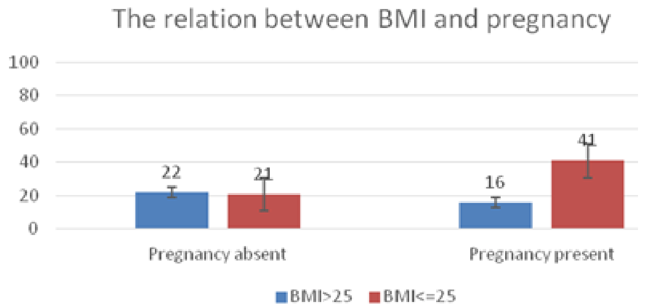

Fig.2. The relation between the BMI values and the presence/ absence of a possible pregnancy

Conclusions

Our study, like other studies, showed that women who have some extra pounds compared to regular women who have ovulation on a regular basis still have much less chance of conceiving a baby, even if they ovulate normally. Of course, the risk of infertility increases proportionally to the extra pounds. Irregular ovulation in women is the most common fertility disorder due to obesity disease.

Although the mechanism by which obesity affects fertility is not well understood and known, there is still an apparent insulin-mediated hyperstimulation of steroid hormone produced by the ovary and a decrease in the amount of globulin-binding sex hormones. Obesity was also associated with an increased risk of losing pregnancy after in vitro fertilization and decreased chance of becoming pregnant.

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