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Reproductive problems and intensity of anxiety and depression in women treated for infertility

Artur Wdowiak[1], Marta Makara-Studzińska[2], Dorota Raczkiewicz[3], Katarzyna Cyranka[4,5]

[1] Diagnostic Techniques Unit, Medical University of Lublin

[2]Department of Health Psychology, Jagiellonian University Medical College

[3.]Institute of Statistics and Demography, Collegium of Economic Analysis, Warsaw School of Economics

[4.]Chair of Psychiatry, Department of Psychiatry, Jagiellonian University Medical College

[5] Chair of Metabolic Diseases, Centre for Advanced Technologies in Diabetes, Jagiellonian University Medical College

Summary

Aim. The aim of the study was to assess the severity of anxiety and depression in women treated for infertility as compared to the severity of these clinical parameters in women without reproductive problems, and to assess the impact of emotional disorders on the ovulation cycle.

Method. Ovulation was assessed by hormonal and ultrasound examinations. The emotional state was examined by the STAI Anxiety State and Trait Inventory and the HADS anxiety and depression scale.

Results. The severity of anxiety as a trait and as a state according to STAI was significantly higher in women treated for infertility than in women with confirmed fertility, as well as higher in women treated for infertility who did not get pregnant than in those who got pregnant. The severity of anxiety and depression were significantly higher in women treated for infertility than in women with confirmed fertility. Women treated for infertility who did not become pregnant had higher severity of depressive symptoms compared to women who were pregnant. In the serum of women treated for infertility, cortisol levels, both during and after ovulation, positively correlated with the severity of anxiety and depression. The same correlations were found in the group of women with confirmed fertility.

Conclusions. (1) Anxiety and depression are associated with human reproductive problems. The nature and direction of the association is to be explored. (2) Emotional disorders adversely affect the secretion of sex cycle hormones and endometrial growth. (3) Couples with reproductive problems require psychological support to improve the effects of infertility treatment.

Key words: infertility, hormones, anxiety, depression

Introduction

Problems with having offspring occur in almost every fifth couple at reproductive age in the European Union [1, 2]. This problem shows an upward tendency, and its causes are very complex. Reproductive disorders are conditioned by both female and male factors [3]. In women, a proper menstrual cycle is responsible, among other things, for their reproductive capacity. Its normal course depends on the undisturbed function of the hypothalamic-pituitary-gonadal axis, additionally regulated by the cerebral cortex. This means that the emotional state of a woman may exert a negative effect on the quality of ovulation, and therefore, on getting pregnant [4].

The occurrence of emotional disorders is associated, among others, with crisis situations which an individual experiences in life, psychological resistance to stress, personality predispositions, culture of life in a given community, and socio-economic conditions. Reproductive problems may be crisis situations in which women experience a high level of stress and emotional disorders. Difficult emotional states experienced in such situation most often include: anxiety, changeability of feelings, irritability, emotional coldness, sadness, and despondency. Studies demonstrate that women who have problems with conception are twice as likely to be affected by emotional disorders than those who are fertile [5]. Moreover, previously existing emotional disorders, such as anxiety and depression, may have a negative effect on the outcome of infertility treatment [6, 7]. The situation of a larger number of cycles of infertility treatments [8] and stopping treatment before becoming pregnant [9] is especially traumatic for couples subjected to assisted reproduction technology.

Although it is well known that an increased level of stress, anxiety and depression exerts a negative effect on fertility in animal models, studies in humans remain incoherent due to individual differences and methodological defects. To-date, attempts to isolate single cause-effect relationships between stress and infertility have remained unsuccessful considering their multi-dimensional etiology. The relationship between reproductive problems and emotional disorders is explained, among others, by the concept of the effect of these disorders on the secretion of sex hormones [4].

The aim of the presented study was evaluation of the severity of anxiety and depression in women treated for infertility, compared to those without reproductive problems, and assessment of the effect of emotional disorders on the course of the menstrual cycle.

Materials and method

Studied group

The study was conducted in 2018 in the gynecology and obstetrics consulting room OVEA in Lublin. The study group included 200 women aged 23−30 with infertility diagnosed according to the WHO criteria. The control group was composed of 100 contemporaries who were confirmed fertile. The control group qualified women who had at least two children, and during the study used the mechanical means of contraception.

In both examined groups, the following women were excluded from the study: those with chronic diseases: metabolic, neurological and cancerous, taking any drugs, dietary supplements, herbal preparations, with exception of folic acid, who had received psychiatric treatment or were participating or had participated in psychotherapy, including during adolescence, with ovulation disorders according to the WHO (Group 1 – hypogonadotropic hypogonadism, Group 2 – polycystic ovary syndrome, Group 3 – premature ovarian failure), and women with BMI below 20 kg/m^2 or over 30 kg/m^2.

The mean age of the women who received treatment for infertility was 26.7 ± 1.9 years, and their age did not significantly differ from the age of the women with confirmed fertility (mean 26.8 ± 1.8 years), (p = 0.790). 17 women from the study group, i.e., 8.5% got pregnant.

The study was voluntary and anonymous. It was performed on the first day of the subjects' ovulation. Consent to participate in the study was obtained from the examined women after previous explanation of its aim and course.

Consent for the research was obtained from the Bioethics Committee at the Medical University in Lublin (No. KE-0254/351/2018).

Method of evaluating the course of menstrual cycle

The course of ovulation was evaluated without hormonal stimulation (hormonal and ultrasound examinations). The USG examination was performed using the ALOKA ProSound SSD 3500 system beginning from day 9 of the cycle until the rupture of the ovarian follicle. The size of the follicle and endometrial thickness were assessed on individual days. From day 9 of the cycle the levels of estradiol, progesterone and luteinizing hormone (LH) were examined. An increase in the level of LH above 10 was adopted as the day of ovulation. On the day of ovulation, thyroid stimulating hormone (TSH) and cortisol levels were additionally examined. On day 7 after ovulation, the levels of estradiol, progesterone and cortisol were determined, and endometrial thickness evaluated using ultrasonography (USG). Anti-Müllerian hormone (AMH) was determined on day 3 of the cycle. The pregnancy in women with the diagnosis of infertility was examined by testing human chorionic gonadotropin (HCG). Blood for hormone tests was collected at the blood collection facility in the OVEA consulting room, Antoniego Szczerbowskiego Street 5, 20-012 Lublin, by an authorized midwife. Blood samples were sent to the Diagnostyka Group authorized laboratory.

Research instruments

State-Trait Anxiety Inventory (STAI) by C.D. Spielberger

This inventory allows the differentiation between anxiety understood as transitory situationally conditioned state of an individual (state anxiety), and anxiety understood as a relatively permanent personality trait (trait anxiety).

The questionnaire consists of two scales: scale X-1 is used for examination of the state anxiety, whereas scale X-2 to examine trait anxiety. Each scale consists of 20 statements.

Hospital Anxiety and Depression Scale (HADS)

This scale is used for self-assessment of the occurrence and severity of anxiety and depressive symptoms. It consists of two independent sub-scales, one of which assesses anxiety (HADS–A), and the other – depression (HADS–D). Each sub-scale contains 7 statements concerning the present status of the examined person [10].

The survey was performed on the day of ovulation.

Statistical methods

Statistical analysis of the data was performed using the statistical software package STATISTICA 13, and the graphs using the Microsoft Excel spreadsheet and STATISTICA 13.

For categorical variables the following parameters were calculated: absolute numbers (n) and relative numbers (ratio between the number of individuals with a given category and the sample size, expressed in %); for continuous variables: minimum and maximum values and arithmetic means (mean, M), reflecting the average level, and standard deviations (standard deviation, SD), measuring the dispersion of the measurements around the arithmetic mean.

Student's t-test for the significance of differences between two mean values in independent samples was applied to compare age, hormone levels, and numerical severity of anxiety and depression between the study and the control groups. Considering large size of the samples, for the study and control groups, normal distribution of the parameter estimators could be assumed, according to the central limit theorem. For comparisons of the severity of anxiety and depression between the groups with and without pregnancy the Mann-Whitney U test was applied, considering a small number of pregnant women. The ranges of severity of anxiety and depression between the study group and the control group, and between the group with pregnancy and the group without pregnancy were investigated using chi-square test of independence. Correlation between hormone levels and severity of anxiety and depression were examined by means of Pearson correlation (r).

Results

Characteristic of menstrual cycle in the examined women

The results of the analysis of menstrual cycle in the examined women are summarized in Table 1.

Table 1. **Menstrual cycle in the examined women**

Variable	IU	Menstrual cycle phase	Study group		Control group		p *	Pregnant (N = 17)		Not pregnant (N = 183)		p#
			M	SD	M	SD		M	SD	M	SD	
Ovulation	Day of cycle		12.41	2.13	12.83	1.54	0.077	13.12	1.96	12.34	2.11	0.064
Endometrial thickness	mm	during ovulation	9.78	1.08	12.84	1.06	<0.001	10.32	1.55	9.73	1.01	0.093
		after ovulation	9.88	1.28	13.01	1.36	<0.001	10.58	1.98	9.82	1.18	0.045
Follicle size	cm	during ovulation	1.86	0.20	1.90	0.25	0.144	1.87	0.27	1.86	0.19	0.775
COR	µg/dl	during ovulation	212.30	40.54	140.72	28.74	<0.001	162.24	19.12	216.95	38.85	<0.001
		after ovulation	216.51	43.63	143.91	34.28	<0.001	163.18	17.58	221.46	42.00	<0.001
AMH	ng/ml	during ovulation	2.47	0.72	2.49	1.00	0.844	2.19	0.52	2.49	0.73	0.122
TSH	µIU/ml	during ovulation	1.76	0.33	1.71	0.43	0.303	1.59	0.60	1.78	0.29	0.823
LH	mIU/ml	during ovulation	27.18	3.91	38.11	5.50	<0.001	28.05	4.32	27.10	3.87	0.528
E2/follicle	pg/ml	during ovulation	206.73	49.93	266.44	52.16	<0.001	279.76	44.06	199.95	44.84	<0.001
		after ovulation	124.83	44.20	140.96	34.76	0.002	187.29	5.41	119.03	41.65	<0.001
PGN	ng/ml	during ovulation	1.01	0.34	1.04	0.37	0.409	1.04	0.39	1.01	0.34	0.921
		after ovulation	18.94	8.15	23.67	3.32	<0.001	24.35	3.53	18.43	8.28	0.012

* comparison between the study group and the control group using Student's t-test

comparison between the group where pregnancy has been achieved and where pregnancy has not been achieved, using Mann-Whitney U test

The day of the ovulation (ovulation on the 12th day of the cycle on average; $p = 0.077$) did not significantly differ between the group of women treated for infertility and the group of women with confirmed fertility, as well as between the group of women treated for infertility who got pregnant and the group of those who did not get pregnant ($p = 0.064$). The women treated for infertility had a significantly thinner endometrium, both during and after ovulation (approx. 10 mm on average), than women with confirmed fertility (approx. 13 mm on average; $p < 0.001$). The women treated for infertility who got pregnant had a significantly thicker endometrium after ovulation (10.58 mm on average) than those who did not get pregnant (9.82 mm on average; $p = 0.045$). The thickness of the endometrium during ovulation did not differ significantly between the group of women treated for infertility who got pregnant and the group of women who did not get pregnant ($p = 0.093$).

The size of the follicle (approx. 1.9 cm on average) during ovulation did not differ significantly between the group of women treated for infertility and the group of women with confirmed fertility ($p = 0.144$) or between the group of women treated for infertility who got pregnant and the group of women who did not get pregnant ($p = 0.775$). The results of ultrasound examinations indicate that the follicle ruptured in 189 women (94.50%) treated for infertility and in 96 women (96.00%) with confirmed fertility (no significant differences between these percentages; $p = 0.574$ for the chi-square test).

The serum cortisol concentration, both during and after ovulation, was significantly higher in women treated for infertility (212 μg/dl and 217 μg/dl on average, respectively) than in women with confirmed fertility (141 μg/dl and 144 μg/dl on average, respectively; $p < 0.001$), as well as in women who did not get pregnant (217 μg/dl and 221 μg/dl on average, respectively) compared with women who got pregnant (162 μg/dl and 163 μg/dl on average, respectively; $p < 0.001$).

Serum concentrations of AMH (over 2 ng/ml on average) and TSH (approx. 1.7 μIU/ml on average) did not differ significantly between the group of women treated for infertility and the group of women with confirmed fertility, or between the group of women treated for infertility who got pregnant and the group of women who did not get pregnant ($p > 0.05$).

Serum LH concentration during ovulation was significantly lower in women treated for infertility (27 mIU/ml on average) than in women with confirmed fertility (38 mIU/ml; $p < 0.001$), and it did not differ significantly between the group of women treated for infertility who got pregnant (28 mIU/ml on average) and the group of women who did not get pregnant (27 mIU/ml on average; $p = 0.528$).

Serum estradiol concentration per follicle, both during and after ovulation, was significantly lower in women treated for infertility (207 pg/ml and 125 pg/ml on average, respectively) than in women with confirmed fertility (266 pg/ml and 141 pg/ml on average, respectively; $p < 0.001$ and < 0.002, respectively), as well as in women treated for infertility who did not get pregnant (200 pg/ml and 119 pg/ml on average, respectively) compared to those who got pregnant (280 pg/ml and 187 pg/ml on average, respectively; $p < 0.001$).

Serum progesterone concentration during ovulation (approx. 1 ng/ml on average,) did not differ significantly between the group of women treated for infertility and the group of women with confirmed fertility ($p = 0.409$) or between the group of women treated for infertility who got pregnant and a group of women who did not get pregnant ($p = 0.921$). However, the serum progesterone concentration after ovulation was significantly lower in women treated for infertility (19 ng/ml on average) than in women with confirmed fertility (24 ng/ml on average; $p < 0.001$), as well as in women treated for infertility who did not get pregnant (18 ng/ml on average) compared with those who got pregnant (mean 24 ng / ml; $p = 0.012$).

Severity of anxiety and depression in the examined women

The severity of trait and state anxiety according to the STAI (Figure 1) was significantly higher in women treated for infertility (about 70 on average) than in women with confirmed fertility (about 13 on average), and also higher in women treated for

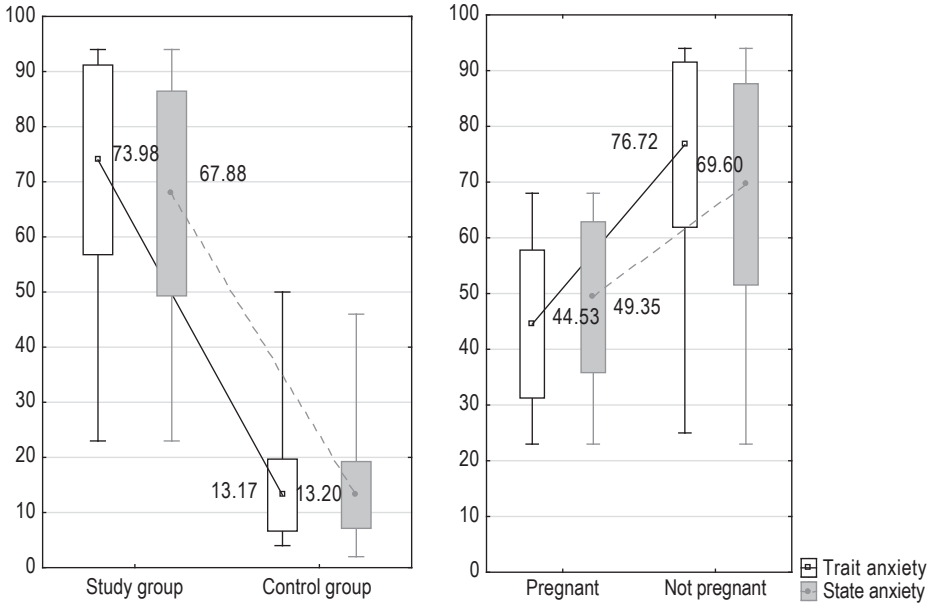

Figure 1. **Severity of trait and state anxiety according to the STAI (in points) in the examined women**

Mean; Mean ± SD; Whisker: Min-Max

Comparison of severity of trait anxiety between the study group and the control group p <0.001; state anxiety p <0.001 (Student's t-test).

Comparison of severity of trait anxiety between women who got pregnant and women who did not get pregnant p <0.001; state anxiety p <0.001 (Mann-Whitney U test).

infertility who did not get pregnant (about 70 on average) compared to those who get pregnant (45 and 49 on average, respectively; p <0.001).

Raw scores for the severity of the symptoms of anxiety and depression according to the HADS (Figure 2) were significantly higher in women treated for infertility (about 12 on average) compared to women with confirmed fertility (5 and 1.5 on average, respectively; p <0.001). The severity of the symptoms of anxiety according to the HADS did not significantly differ between the group of women treated for infertility whom got pregnant (11.65 on average) and the group of women whom did not get pregnant (11.91 on average; p = 0.534). Raw scores or the severity of the symptoms of depression according to the HADS were significantly higher in women treated for infertility who did not get pregnant (12.37 on average) compared to those who got pregnant (9.41 on average; p = 0.001).

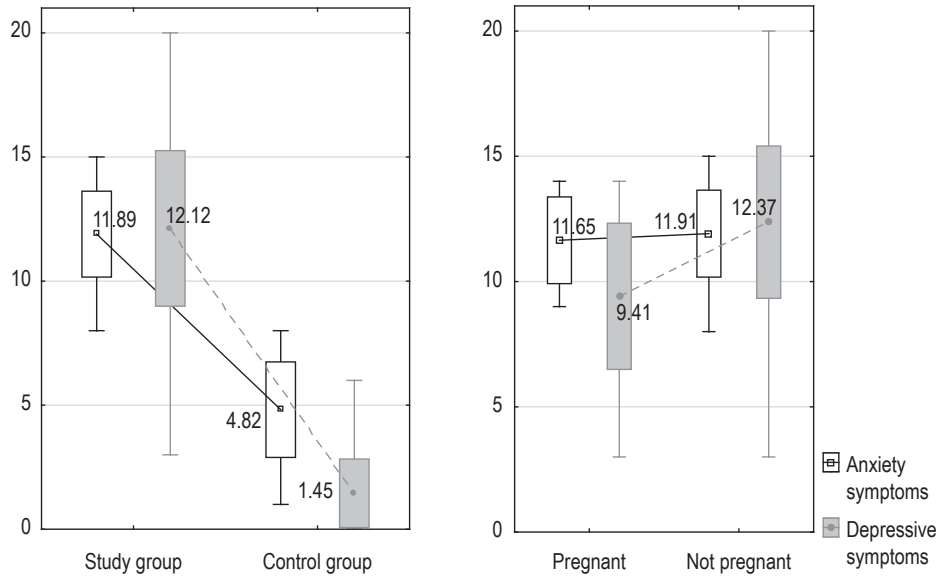

Figure 2. **Severity of anxiety and depressive symptoms according to the HADS (in points) in the examined women**

Mean; Mean ± SD; Whisker: Min-Max

Comparison of severity of anxiety symptoms between the study group and the control group p <0.001; depressive symptoms p <0.001 (Student's t-test).

Comparison of severity of anxiety symptoms between women who got pregnant and women who did not get pregnant p = 0.534; depressive symptoms p=0.001 (Mann-Whitney U test).

After grouping the raw results of the severity of trait and state anxiety according to the STAI into severity intervals, significant differences may also be seen between the group of women treated for infertility and the group of women with confirmed

fertility, as well as between the group of women treated for infertility who did not get pregnant and those who got pregnant (Figure 3). A significantly greater percentage of women treated for infertility had moderate or severe trait and state anxiety, and a significantly lower percentage – mild trait and state anxiety compared to the group of women with confirmed fertility.

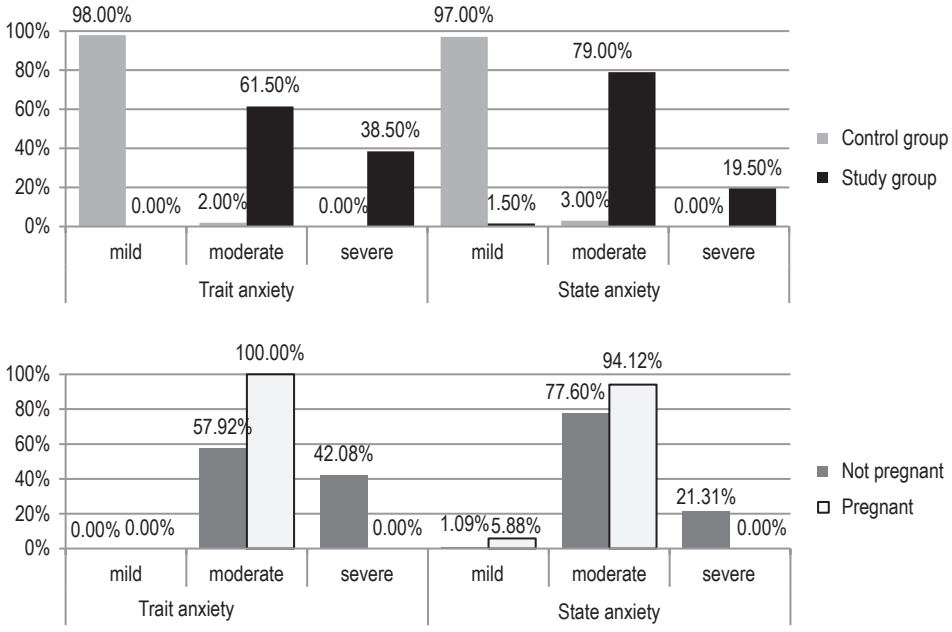

Figure 3. **Severity of trait and state anxiety according to the STAI (% of women)**

Comparison of severity of trait anxiety between the study group and the control group p <0.001; state anxiety p <0.001 (chi-square test).

Comparison of severity of trait anxiety between women who got pregnant and women who did not get pregnant p = 0.003; state anxiety p = 0.038 (chi-square test).

Severe trait and state anxiety was present only in women treated for infertility who did not get pregnant (42% and 21%, respectively). All women treated for infertility who got pregnant had moderate trait anxiety, and 94% of them had moderate state anxiety.

The results of the severity of anxiety and depressive symptoms according to the HADS are presented in Figure 4. All women with confirmed fertility had mild anxiety symptoms, while 76% of women treated for infertility had moderate, and 22.5% of them had severe anxiety symptoms. Depressive symptoms did not occur in 29% of women with confirmed fertility, 71% of them had mild depressive symptoms, and none of them had moderate or severe depressive symptoms. On the other hand, 70% of women treated for infertility had moderate depressive symptoms, 22% – severe, 8% – mild, and none of the women had no such symptoms.

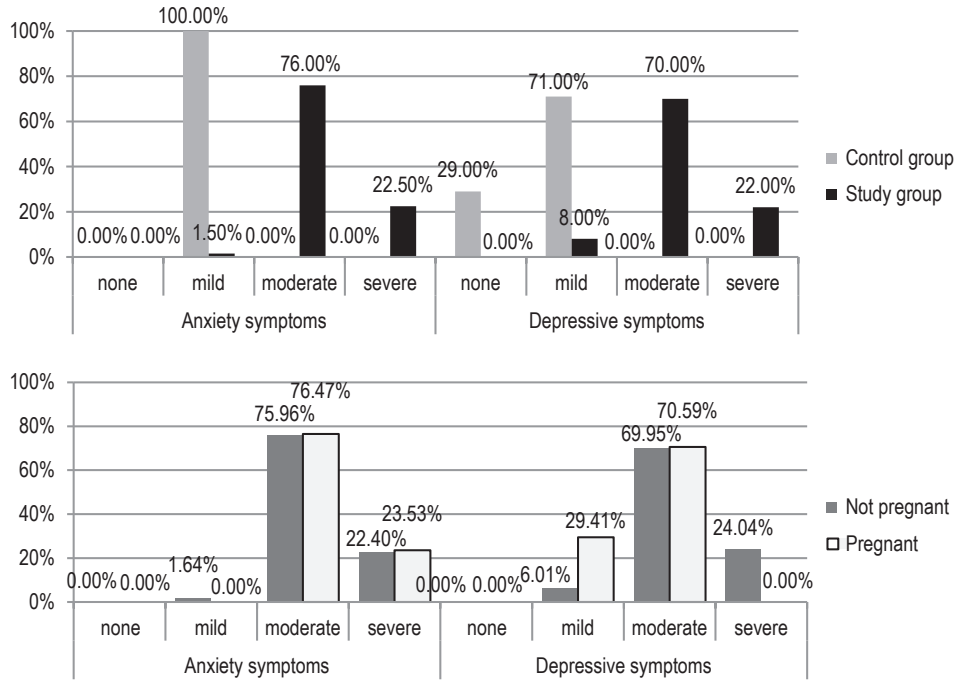

Figure 4. **Severity of anxiety and depressive symptoms according to the HADS (% of women)**

Comparison of severity of anxiety symptoms between the study group and the control group p <0.001; depressive symptoms p <0.001 (chi-square test).

Comparison of severity of anxiety symptoms between women who got pregnant and women who did not get pregnant p = 0.866; depressive symptoms p = 0.002 (chi-square test).Porównanie nasilenia objawów lękowych między kobietami, u których uzyskano ciążę, a kobietami, u których nie uzyskano ciąży p = 0,866; depresyjnych p = 0,002 (test chi-kwadrat).

24% of women treated for infertility who did not get pregnant had severe depressive symptoms, 71% – moderate, and 6% – mild. On the other hand, among women treated for infertility who get pregnant, 29% had mild depressive symptoms, 70% – moderate, but none of them had severe depressive symptoms.

Severity of anxiety and depression and hormone serum concentration in the examined women

The correlations between the severity of anxiety and depressive symptoms and the concentrations of hormones in the serum of the examined women are presented in Table 2. In the serum of the women treated for infertility, the cortisol concentration, both during and after ovulation, positively correlated with the severity of trait and state anxiety, as well as the symptoms of anxiety and depression. The same correlations were observed in the group of women with confirmed fertility (with the exception of symptoms of anxiety).

Table 2. **Correlations between the severity of anxiety and depression (in points) and hormone serum concentration in the examined women**

Hormones	Menstrual cycle phase	Study group								Control group							
		STAI – anxiety				HADS – symptoms				STAI – anxiety				HADS – symptoms			
		trait		state		anxiety		depression		trait		state		anxiety		depression	
		r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
COR (µg/dl)	during ovulation	0.615	<0.001	0.708	<0.001	0.300	<0.001	0.703	<0.001	0.454	<0.001	0.422	<0.001	0.100	0.324	0.302	0.002
	after ovulation	0.607	<0.001	0.737	<0.001	0.351	<0.001	0.744	<0.001	0.490	<0.001	0.470	<0.001	0.092	0.361	0.366	<0.001
LH (mIU/ml)	during ovulation	−0.183	0.009	−0.162	0.022	−0.166	0.019	−0.071	0.320	−0.335	0.001	−0.140	0.166	0.012	0.903	−0.291	0.003
E2/follicle (pg/ml)	during ovulation	−0.641	<0.001	−0.646	<0.001	−0.279	0.000	−0.643	<0.001	−0.171	0.089	−0.122	0.228	−0.069	0.498	−0.112	0.270
	after ovulation	−0.709	<0.001	−0.714	<0.001	−0.277	0.000	−0.673	<0.001	−0.078	0.444	−0.323	0.001	−0.063	0.534	−0.202	0.044
PGN (ng/ml)	during ovulation	−0.078	0.270	0.003	0.971	−0.017	0.816	0.008	0.909	0.061	0.545	−0.031	0.763	−0.095	0.347	−0.122	0.227
	after ovulation	−0.378	<0.001	−0.639	<0.001	−0.283	<0.001	−0.626	<0.001	−0.135	0.180	−0.081	0.422	−0.203	0.043	−0.325	0.001

The LH concentration during ovulation negatively correlated with the severity of trait and state anxiety and the symptoms of anxiety in women treated for infertility, as well as with the severity of state anxiety and the symptoms of depression in women with confirmed fertility. However, no correlation was found between the LH concentration and: severity of the symptoms of depression in women treated for infertility, severity of state anxiety and the symptoms of anxiety in women with confirmed fertility.

In the serum of women treated for infertility, the estradiol concentration, both during and after ovulation, negatively correlated with the severity of trait and state anxiety, and the symptoms of anxiety and depression. In turn, in women with confirmed fertility the estradiol concentration per follicle after ovulation negatively correlated with the severity of state anxiety and the symptoms of depression. In this group, no correlation was found between the estradiol concentration and the results of the HADS and STAI. No correlation was observed between the progesterone concentration during ovulation and the results of the HADS and STAI in both women treated for infertility and those with confirmed fertility. However, the progesterone concentration after ovulation negatively correlated with the severity of trait and state anxiety, and the symptoms of anxiety and depression in women treated for infertility, and with the severity of the symptoms of depression in women with confirmed fertility. In this group, no correlation was found between the progesterone concentration after ovulation and the severity of trait and state anxiety, and the symptoms of anxiety.

Discussion

The study showed that the emotional state of women subjected to infertility therapy was worse than that of their contemporaries having offspring. In women with reproductive problems, the severity of emotional disorders was higher than in those with confirmed fertility. Similar observations are described in international literature; however the reports concerning this problem are ambiguous. Some studies confirmed profound reproductive consequences of emotional disorders [11–16], whereas others showed a small effect or lack of relationship [17–23].

Smeenk et al. [8] indicate that anxiety and depression are significantly negatively correlated with the outcome of pregnancy in a multi-centre perspective study in 2001. The same group of researchers were not able to repeat this conclusion in the subsequent study conducted in 2009 [9]. Studies published by Chi et al. [24] and Ramezanzadeh et al. [25] demonstrated that reproductive problems exert a negative effect on the quality of life, leading to anxiety, depression, isolation, frustration, sense of unattractiveness, and may also cause identity disorders. The results of these studies are coherent with those conducted in Iran, where it was found that women with reproductive disorders experienced more severe depression, compared to infertile men [26]. Studies carried out in Japan confirmed that an increased depression and anxiety in women subjected to infertility therapy may result from the lack of support on the part of their spouses and the experienced stress [27].

Bolsoy et al. [28] conducted research in a group of 248 patients with the diagnosis of infertility in Turkey and showed that the quality of life in the physical, psychological and social domains did not differ between infertile women and infertile men. However, the results in the environmental domain were considerably higher in infertile women than men [28]. Differences observed in the results of studies conducted in many places worldwide may be conditioned by religious, cultural and economic differences in particular countries. Nevertheless, these studies demonstrate that the cause of emotional disorders among women treated for infertility may be a decrease in their quality of life in various spheres.

Lakatos et al. [29], in their studies conducted in Hungary, obtained results similar to those in the presented study. The study was carried out in a group of 225 women (134 with primary infertility and 91 fertile), where a higher level of depression measured using the BDI, as well as higher STAI values, were observed among women with reproductive disorders. However, in the presented study, women treated for infertility had higher STAI values, compared to the study by Lakatos et al. [29].

Based on the results obtained in this study, it may be presumed that during infertility therapy women with less severe anxiety and depression got pregnant more often. Similar relationships were described by Terzioglu et al. [30] who, using the STAI and BDI questionnaires, examined 217 women treated for infertility in Turkey. The researchers confirmed that a greater severity of anxiety and depression during therapy occurred in women who did not get pregnant. Other studies demonstrated that emotional disorders in patients treated by *in vitro* fertilization method were accompanied by a lower percentage of obtained pregnancies [11–13, 16, 31]. However, there are also researchers who presented opposite results of research, and postulated a small effect or lack of relationship between emotional disorders and getting pregnant during infertility treatment [18–22].

The presented study demonstrated that the severity of the symptoms of anxiety and depression among women with confirmed fertility, as well as those trying to get pregnant, increases the secretion of cortisol, which is in accordance with the reports presented in numerous reports [e.g., 32, 33]. In the serum of women treated for infertility, the level of estradiol decreased under the effect of the severity of trait and state anxiety, and the symptoms of anxiety and depression. This decreased secretion of estradiol may be the result of stress-induced suppression of the release of pituitary gonadotropins, and also the direct effect of glucocorticoids and sympathetic innervation on the activity of gonads, which is confirmed by scientific reports [34]. The inhibitory effect of stress is initiated by corticotropin-releasing hormone (CRH) – mediating the suppression of the gonadotropin-releasing hormone (GnRH) pulse generator and reducing the subsequent pituitary gonadotropin release described in rats [35], in sheep [6], in non-human primates [37], as well as in humans [38].

In Poland, the importance of psychological parameters in the context of lack of children was studied by Kalus and Szymańska [39]. The participants postponed taking on parental roles for a specified time or declared voluntary childlessness. The analysis

showed that significant relationships exist between family assessment and: life satisfaction (in men), marital satisfaction (in women) and attitudes towards children (in both genders). The research revealed that both the quality of family relationships and gender play an important role in shaping procreative attitudes of spouses who do not take parental roles.

In the present study, the level of LH during ovulation decreased under the effect of trait and state anxiety and the symptoms of anxiety in women treated for infertility, as well as with the severity of trait anxiety and the symptoms of depression in women with confirmed fertility. This is confirmed by other studies [40, 41], which showed that the level of glucocorticoids caused by exposure to stress may reduce the release of sex steroids in association with the reduction of serum LH level.

Based on the results of the present study, it was found that the endometrial thickness was greater in women who got pregnant, than in those who did not get pregnant while trying to get pregnant naturally. Similar observations were made by Griesinger et al. [42] who proved that endometrial thickness is a prognostic factor in getting pregnant in the *in vitro* fertilization procedure. In their studies, EMT (endometrial thickness) indeed is an independent factor affecting outcome, this finding implies that at a baseline live birth rate of 20% an increase of 2 mm in EMT should result in an increase of the live birth rate of ~1.6%. This was not confirmed by the study by Barros Delgadillo et al. [43] conducted among couples trying to become pregnant by intrauterine insemination.

The current study demonstrated the importance of the role of a proper level of progesterone in getting pregnant naturally. Similar relationships were described in other studies [44, 45] among women who got pregnant due to IVF. The effect of the level of progesterone on getting pregnant was also confirmed by a study of the level of this hormone in follicular fluid, where higher values of this hormone were a prognostic factor in getting pregnant, which may play an important role in regulating oocyte developmental potential [46].

The observed stress-related disorders in the secretion of hormones, and consequently, an insufficient development of the endometrium in the sexual cycle, seem to explain an unfavorable effect on the chance of getting pregnant naturally. However, studies on animal models indicated that chronic, unpredictable stress in mice also weakens the potential for oocyte development by acute apoptosis and oxidative stress [47–49]. Therefore, it would be justifiable to conduct further studies within a wider scope in the future concerning the effect of emotional factors on fertility.

The results of own study suggest that an approach to women who are treated for reproductive problems should be verified [50]. A specialist in gynecology taking care of an infertile couple is not able on his own to diagnose and treat emotional disorders; hence, cooperation with a psychologist and psychiatrist is very important. Undoubtedly, the problem requires further research carried out in a larger group of women. These studies could contribute to the introduction of more comprehensive programs of action on behalf of prophylaxis and therapy of emotional disorders in women with reproductive problems.

A limitation of the study is the large disproportion in the number between the group of women who did not get pregnant and the group of women who got pregnancy. This is because natural efforts to get pregnant are on average 10% effective. Such numbers in statistical analysis made it impossible to use parametric tests and forced the use of non-parametric tests to compare quantitative features between the two groups.

Conclusions

1. Severity of anxiety and depression may be one of the causes of human reproductive problems.
2. Emotional disorders exert an unfavorable effect on the secretion of sex cycle hormones and endometrial growth.
3. Couples with reproductive problems require psychological support in order to improve the outcomes of treatment of infertility.

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Address: Katarzyna Cyranka
Department of Psychiatry
Chair of Psychiatry, Jagiellonian University Medical College
Chair of Metabolic Diseases, Jagiellonian University Medical College
31-501 Kraków, Kopernika Street 21A
e-mail: katarzyna.cyranka@gmail.com