



THE RELATIONSHIP BETWEEN FERTILITY DISORDERS AND DEPRESSION IN WOMEN – REVIEW

Carlo Bienkowski¹, Monika Kowalczyk¹, Konrad Zasadzinski¹, Agata Golik¹, Joanna Kacperczyk-Bartnik^{2#}, Pawel Bartnik², Agnieszka Dobrowolska-Redo², Ewa Romejko-Wolniewicz²

1. Student's Scientific Group affiliated to 2nd Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland
2. 2nd Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland

#Corresponding author: Joanna Kacperczyk-Bartnik, 2nd Department of Obstetrics and Gynaecology, Medical University of Warsaw, Karowa 2 St, 00-315 Warsaw, Poland, phone number: +48225966421, e-mail: asiakacperczyk@gmail.com

RUNNING TITLE	Fertility disorders and depression
KEYWORDS	fertility disorders; depression; psychiatry; gynaecology
WORD COUNT	1533
CONFLICT OF INTERESTS	no conflicts of interest

ABSTRACT

Depression is defined by the WHO as persistent sadness and loss of interest in taking actions that usually brought joy accompanied by the inability to undertake basic activities during the day for at least two weeks. Infertility is defined by the WHO as the inability to get pregnant despite regular sexual intercourse (3-4 times a week), maintained > 12 months, without the use of any contraceptive methods. This review presents reports from the field of gynaecology and psychiatry regarding both depression and infertility, and association between these conditions. The most important conclusions from this association have been analysed and summarized in this review. Some reports indicated an increased percentage of infertility in patients suffering from depression. On the other hand, depression may also increase due to infertility, which leads to a vicious circle. Depression may also lead to decreased libido. Holistic approach to patients managed because of infertility is recommended, including screening for depressive disorders.

BACKGROUND

The definition of depression according to the World Health Organization (WHO) states that depression is a common mental disorder, characterized by persistent sadness and loss of interest in activities that were previously found enjoyable, accompanied by an inability to carry out daily activities, lasting for at least two weeks [1]. Depression is the fourth most serious health problem in the world. The WHO estimates that by 2020 depression will become the world's second most common cause of disability resulting from health condition [2]. DSM-5 reports that depressive disorders are among the most prevalent categories of mental disorders. When it comes to specific depressive disorders, the prevalence of major depressive disorder is around 16%, and the monthly prevalence of this disorder reaches 6%. DSM-5 includes eight different depressive disorders, each with its own diagnostic criteria. Although a major depressive disorder begins with a single episode, 50% of patients will come back before the end of the year, and as many as 85% will experience a relapse during their lifetime. A larger depressive disorder usually lasts about 6 months, with 20% of the episodes becoming chronic. The prevalence of depressive disorders is greater among women. In addition, suicide attempts are also more common in women, but the risk of suicide is lower in women [3].

Infertility is currently defined by the WHO as the inability to get pregnant despite regular sexual intercourse (3-4 times a week), maintained over 12 months, without any precautionary measures [4]. The disease, according to the WHO, is the reverse of health, which defines it as a state of complete well-being (physical, mental and social well-being), and not just the absence of disease or ill-treatment. In this approach, the disease is a condition that is contrary to health, the disease is a lack of health and the disease is a condition of disability, disability and/or discomfort. Based on the WHO definition of health, a 1994 definition was developed at the International Conference on Population and Development (ICPD) in Cairo for the definition of reproductive health, which presupposes that it is a state of physical, mental and social well-being in all matters related to the reproductive system [5].

Infertility, infertility therapy and mental disorders are interrelated in a very complex way in the field of mutual etiopathogenic determinants. The presence of mental disorders can affect fertility, while the diagnosis of infertility may trigger the development of mental disorders related to stress or adaptation problems [6, 7]. Researchers look for similar associations in the field of the influence of symptoms of mental disorders (mainly depression and anxiety) on the results of infertility treatment [8]. This also applies to the relationship between the lack of effects of assisted reproduction procedures and the development of symptoms of mental disorders in both sexes [9].

MATERIAL AND METHODS

This review presents reports from the fields of gynaecology and obstetrics and psychiatry regarding

both depression and fertility disorders, and how the two diseases are related to each other. To search for publications, the medical databases of PubMed and UpToDate were used. The World Health Organization website was also used. Phrases of 'fertility disorders', 'depression', 'treatment of depression', 'treatment of fertility disorders', 'depression fecundity' and 'depression and impaired fertility' were searched. The most important conclusions from this association have been analysed and summarized in this review.

PUBLIC HEALTH PICTURE

Mental disorders have been increasingly portrayed by the WHO and researchers as a growing burden to global public health. Just the sheer economic impact of mental disorders is significant; it is expected to cost almost a third of the projected US\$47 trillion incurred by all non-communicable diseases by 2030 [7]. The WHO now ranks depression as one of the most burdensome diseases in the world, and the organization has projected and warned that depression is predicted to be the highest-ranked disease problem in the developed world by 2020 [8]. It has been anticipated that depression and anxiety are expected to be the most common illnesses by the end of the century, especially among women [9]. The number of inhabitants of the WHO European Region suffering from depressive disorders reaches 40 million, and the disease prevalence rates in individual countries range from 3.8% to 6.3% of the total population, according to the data published by the WHO for 2015 [10]. The total annual cost of depression in Europe was estimated at Euro 118 billion in 2004, which corresponds to a cost of Euro 253 per inhabitant [11].

The study of infertile couple has always been focused on different factors: ovulatory factor (present in about 20% of couples), utero-tubal peritoneal factor (present in about 30% of couples), semen migration factor (10% of cases) and male factor (30% of couples). Around 40% of all infertile couples exhibit a combination of factors and about 15% of couples may not display any objective alteration leading to a definite diagnosis [12].

DISCUSSION

The inability to conceive and give birth is a universal stressor in every culture associated with additional stress [13]. Initially, a woman (and her partner), cope with the inability to get pregnant. After a period of failures, usually 12-18 months, many couples decide to undergo diagnostic process and treatment [14]. The process of medical diagnosis, followed by non-invasive or invasive treatment trigger another group of tensions, which are important causes of stress contributing to its escalation. Women also have to face very strong challenges after unsuccessful treatment attempts. It is emphasized that the intensity of stress in such a difficult situation is closely related to the woman's desire, and indirectly to her partner's. The more patients wish to become parents, the higher level of experienced stress is encountered. Stress triggers the coping process including cognitive and behavioural efforts aimed at overcoming the problem and regulating unpleasant emotions [15].

The diagnosis of infertility is associated with a significant violation of women's self-esteem and leads to dissatisfaction [16, 17]. Women suffering from infertility, feel overwhelmed by difficulties in social relations and exposure to social pressure. There is an increased risk of developing relationship problems such as guilt, sexual dysfunction or fear of abandonment [18]. Women also experience existential doubts as they may feel the sense of their own existence becomes threatened. Reproductive difficulties make women to experience intense emotional reactions, mainly sadness and anxiety. After getting familiar with the diagnosis, life satisfaction and quality of life are reduced [19]. Long-term suffering is associated with strong negative emotions, such as shock and denial, rebellion, feelings of harm, lost or uncertainty. It should be remembered that these emotions accompany women for many months and sometimes years [20]. Women also report feeling of guilt, loss, and often extreme loneliness. These experiences are accompanied by feelings of sadness, despair, emptiness, fear and uncertainty. Psychological effects associated with infertility treatment may lead to depressed mood, and finally - to depression [21, 22, 23, 24].

Whereas fertility disorders can be a major risk factor for mood disorders including depression, it still remains controversial, whether depression itself may contribute to infertility as its direct cause. Study in this field remains inconclusive with some reports showing a statistically significant positive correlation between the intensity of depressive symptoms and infertility rates and others showing no such relationship [25, 26, 27]. Scarce research focused on fecundity of female patients diagnosed with depression shows similar fertility rates in these women compared to the general population [28].

There is, however, some evidence for psychological factors influencing the success rate of artificial reproductive technology (ART) procedures [29, 30, 31]. A 2014 cohort study on 501 US-women investigated the relationship between salivary alpha-amylase levels as a biomarker of stress and pregnancy rates following ART procedures. Women in the highest tertile of alpha-amylase levels were found to have a 29% decrease in fecundity compared with women in the lowest tertile [32]. A similar study on 135 in vitro fertilization (IVF) patients was focused on salivary and hair cortisol levels (the latter corresponding to its blood levels in the prior 3 to 6 months), another important biomarker of psychological stress. Chronic elevation of cortisol levels prior to IVF treatment was associated with a reduction of pregnancy rates ($p=0.017$) [33].

While these studies do not give us any definitive answers regarding causation, they were able to prove a significant correlation between stress levels in women (tested objectively) and their fertility. Interventions focused on diminishing these levels, i.e. alleviating psychological symptoms, including mood disturbances and depression could improve reproductive outcomes in women with fertility disorders [34]. It is important to note that newer studies including a 2018 meta-analysis investigating subjective methods of depressive symptoms assessment (self-reported questionnaires) did not show any association between depression scores and ART outcomes [26, 35].

CONCLUSIONS

Both fertility disorders and depression are significant public health problems. The results of scientific reports on the relationship between infertility and depression are ambiguous, but they confirm a direct causal relationship between infertility in the development of depression, while not all confirm, and some even rule out a causal relationship between depression and fertility disorders. What we know for sure is that depression significantly affects the failure in the use of assisted reproduction techniques. As both diseases more or less affect each other, and can become more intense, they should be diagnosed and treated early to ensure the well-being of the patient.

CITE THIS AS

MEDtube Science Jun, 2019, Vol. VII (2), 20 – 23

ABBREVIATIONS

ART – artificial reproductive technology
ICPD – International Conference on Population and Development
IVF – in vitro fertilization
WHO – World Health Organization

REFERENCES

1. World Health Organization. Depression: let's talk. Available from: https://www.who.int/mental_health/management/depression/en/. Accessed: 23rd February 2019.
2. World Federation for Mental Health. Depression: a global crisis. Available from: https://www.who.int/mental_health/management/depression/wfmh_paper_depression_wmhd_2012.pdf. Accessed: 23rd February 2019.
3. Vijayakumar L. Suicide in women. *Indian J Psychiatry* 2015;57(Suppl 2):S233–S238.
4. World Health Organization. Infertility is a global public health issue. Available from: <https://www.who.int/reproductivehealth/topics/infertility/perspective/en/>. Accessed: 23rd February 2019.
5. United Nations. Report of the International Conference on Population and Development. Available from: http://www.un.org/en/development/desa/population/events/pdf/expert/27/SupportingDocuments/A_CONF.171_13_Rev.1.pdf. Accessed: 23rd February 2019.
6. Rooney KL, Domar AD. The relationship between stress and infertility. *Dialogues Clin Neurosci* 2018;20(1):41-47.
7. Bloom DE, Cafiero ET, Jane-Llopis E et al. The Global Economic Burden of Noncommunicable Diseases. Geneva: World Economic Forum; 2011.
8. World Health Organization. Promoting Mental Health: Concepts, Emerging Evidence, Practice: A Summary Report/A Report From the World Health Organization, Department of Mental Health and Substance Abuse in Collaboration with the Victorian Health Promotion Foundation (VicHealth). Geneva: World Health Organization; 2004.

9. Bansal P, Chaudhary A, Soni RK, Sharma S, Gupta VK, Kaushal P. Depression and anxiety among middle-aged women: A community-based study. *J Family Med Prim Care* 2015;4:576-81.
10. World Health Organization. 3 out of 4 people suffering from major depression do not receive adequate treatment. Available from: http://www.euro.who.int/en/media-centre/sections/press-releases/2017/3-out-of-4-people-suffering-from-major-depression-do-not-receive-adequate-treatment?fbclid=IwAR1P87h5C4Q5SXLrZ2tzCg6_7TVcSpdWeD7uINO3LPsGyCBBkldOi5ojvY. Accessed: 23rd February 2019.
11. Sobocki P, Jonsson B, Angst J, Rehnberg C. Cost of depression in Europe. *J Ment Health Policy Econ*. 2006;9(2):87-98.
12. Brugo-Olmedo S, Chillik C, Kopelman S. Definition and causes of infertility. *Reprod Biomed Online* 2001;2(1):41-53.
13. Holka-Pokorska JPH, Marek Jarema MJ, Adam Wichniak AW. Clinical determinants of mental disorders occurring during the infertility treatment. *Psychiatr Pol* 2015;49(5):965-982.
14. Chen TH, Chang SP, Tsai CF, Juang KD. Prevalence of depressive and anxiety disorders in an assisted reproductive technique clinic. *Hum Reprod* 2004;19(10):2313-8.
15. Klemetti R, Raitanen J, Sihvo S, Saarni S, Koponen P. Infertility, mental disorders and well-being: a nationwide survey. *Acta Obstet Gynecol Scand* 2010;89(5):677-682.
16. Vitale SG, La Rosa VL, Petrosino B, Rodolico A, Mineo L, Lagana AS. The Impact of Lifestyle, Diet, and Psychological Stress on Female Fertility. *Oman Med J* 2017;32(5):443-444.
17. Taylor A. ABC of subfertility: extent of the problem. *BMJ* 2003;327(7412):434-436.
18. Kinner VL, Het S, Wolf OT. Emotion regulation: exploring the impact of stress and sex. *Front Behav Neurosci* 2014;8:397.
19. Cizmeli C, Lobel M, Franasiek J, Pastore LM. Levels and associations among self-esteem, fertility distress, coping, and reaction to potentially being a genetic carrier in women with diminished ovarian reserve. *Fertil Steril* 2013;99(7):2037-44.e3.
20. Poddar S, Sanyal N, Mukherjee U. Psychological profile of women with infertility: A comparative study. *Ind Psychiatry J* 2014;23(2):117-126.
21. Tabong PT, Adongo PB. Infertility and childlessness: a qualitative study of the experiences of infertile couples in Northern Ghana. *BMC Pregnancy Childbirth* 2013;13:72.
22. Yari F, Moghadam ZB, Parvizi S, Nayeri ND, Rezaei E. Sexual and reproductive health problems of female university students in Iran: a qualitative study. *Glob J Health Sci* 2015;7(4):278-285.
23. Charles ST, Carstensen LL. Social and emotional aging. *Ann Rev Psychol* 2010;61:383-409.
24. Lakatos E, Szigeti JF, Ujma PP, Sexty R, Balog P. Anxiety and depression among infertile women: a cross-sectional survey from Hungary. *BMC Womens Health* 2017;17(1):48.
25. Nillni YI, Wesselink AK, Gradus JL. Depression, anxiety, and psychotropic medication use and fecundability. *Am J Obstet Gynecol* 2016;215(4):453.e1-8.
26. Evans-Hoeker EA, Eisenberg E, Diamond MP et al. Major depression, antidepressant use, and male and female fertility. *Fertil Steril* 2018;109(5):879-887.
27. Lynch CD, Sundaram R, Buck Louis GM et al. Are increased levels of self-reported psychosocial stress, anxiety, and depression associated with fecundity? *Fertil Steril* 2012;98(2):453-458.
28. Tondo L, Baldessarini RJ. Fertility Rates in Patients With Mood Disorder in Sweden and Sardinia. *JAMA Psychiatry* 2013;70(10):1115.
29. Rooney KL, Domar AD. The relationship between stress and infertility. *Dialogues Clin Neurosci* 2018;20(1):41-47.
30. Matthiesen SM, Frederiksen Y, Ingerslev HJ et al. Stress, distress and outcome of assisted reproductive technology (ART): a meta-analysis. *Hum Reprod* 2011;26(10):2763-2776.
31. El Kissi Y, Ben Romdhane A, Hidar S et al. General psychopathology, anxiety, depression and self-esteem in couples undergoing infertility treatment: a comparative study between men and women. *Eur J Obstet Gynecol Reprod Biol* 2013;167(2):185-189.
32. Lynch CD, Sundaram R, Maisog JM et al. Preconception stress increases the risk of infertility: results from a couple-based prospective cohort study—the LIFE study. *Hum Reprod* 2014;29(5):1067-1075.
33. Massey AJ, Campbell BK, Raine-Fenning N, Pincott-Allen C, Perry J, Vedhara K. Relationship between hair and salivary cortisol and pregnancy in women undergoing IVF. *Psychoneuroendocrinology* 2016;74:397-405.
34. Frederiksen Y, Farver-Vestergaard I, Skovgard NG, Ingerslev HJ, Zachariae R. Efficacy of psychosocial interventions for psychological and pregnancy outcomes in infertile women and men: a systematic review and meta-analysis. *BMJ Open* 2015;5(1):e006592.
35. Purewal S, Chapman SCE, van den Akker OBA. Depression and state anxiety scores during assisted reproductive treatment are associated with outcome: a meta-analysis. *Reprod Biomed Online* 2018;36(6):646-657.



sharing
medical
knowledge™