The association between women loss of reproduction capacity and depressive disorder: a selective literature review

Reprodukcinių savybių praradimo sąsaja su depresiniu sutrikimu: selektyvi literatūros apžvalga

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SUMMARY

Infertility is a disease of the reproductive system defined as the inability to reach clinical pregnancy for 12 months or more through regular sexual intercourse without using protection. It is well known that for most women, failure to conceive a child is the most difficult emotional experience. The risk is exacerbated by the public perception that infertility is caused by women, especially in developed countries, where having children is important for religious, social, cultural and economic reasons. Therefore, infertility can affect their social, physical and psychological well-being and lead to social isolation. Infertile patients often complain of stress and affective disorders, of which anxiety and depressive disorders (because of the infertility or infertility treatment) are the most common.

Key words: infertility, depression, anxiety, assisted reproductive technology, infertility treatment

SANTRAUKA

Reprodukcinių savybių praradimas (nevaisingumas) – tai reprodukcinės sistemos liga, apibrėžiama kaip nesugebėjimas pasiekti klinikinio nėštumo 12 ir daugiau mėnesių reguliarių lytinių santykių metu, nenaudojant apsauginių priemonių. Gerai žinoma, kad daugumai moterų negebėjimas pastoti ir pagimdyti vaiką – sunkiausias emocinis išgyvenimas. Riziką didina visuomenės suvokimas, kad negalėjimas susilauti vaiko kyla dėl moters kaltės, ypač išsivysčiusiose šalyse, kur vaikų turėjimas yra svarbus dėl religinių, socialinių, kultūrinių ir ekonominių priežasčių. Dėl šių priežasčių nevaisingumas turi įtakos moters socialinei, fizinei ir psichologinei savijautai bei gali sukelti socialinę izoliaciją. Nevaisingos pacientės dažnai skundžiasi streso bei afektiniais sutrikimais, iš kurių dažniausi yra nerimo ir depresinis (sukeltas nevaisingumo ar nevaisingumo gydymo) sutrikimas.

Raktiniai žodžiai. Nevaisingumas, depresija, nerimas, pagalbinis apvaisinimas, neivaisingumo gydymas

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INTRODUCTION

Infertility is a condition of the reproductive system, defined as the inability to achieve clinical pregnancy for 12 months or more during regular sexual intercourse without the use of protective measures. It is divided into primary, when there have been no previous pregnancies, and secondary, when there has been at least one successful, uninterrupted pregnancy [1]. According to PSO global study in 2012 (190 countries and their territories were involved), 48.5 million couples were affected by infertility in 2010. 14.4 million of these couples live in South Asia, and further 10.0 mln. live in Sub-Saharan Africa. In Central/Eastern Europe and Central Asia, the number of infertile couples is looking for 3.8mln. [2]. Infertility affects about 10–15% couples or approximately every seventh couple [3]. In Lithuania in 2018, the number of infertile women per 1,000 population reached 1.59, men – 0.13 [4]. In most cases, couples learn about infertility only after long-term attempts to conceive.

Although infertility is considered a stressful situation for a couple, women still experience more stress than men [5]. For most women, the inability to give birth is the most difficult emotional experience, causing the same level of psychological stress as a person with oncological or ischemic heart disease [6]. Studies examining gender differences in psychological adjustment to infertility have found that women in such traumatic situations are at higher risk of developing mental disorders [7]. The risk is exacerbated by the public perception that infertility is caused by women, especially in developed countries, where having children is important for religious, social, cultural and economic reasons [8]. Therefore, infertility can affect their social, physical and psychological well-being and lead to social isolation.

Depressive disorder is one of the most common mental health disorders in infertile women, primarily due to loss of reproductive traits, as well as stressful assisted reproduction procedures and adverse outcomes of assisted reproduction procedures [9].

The increasing prevalence of infertility in society and the negative impact on psychological and social well-being have led us to review the links between infertility, infertility treatment, and depressive disorder

The objective of the present report was to review the association between infertility, infertility treatment, and depressive disorder based on national and international literature.

METHODS

MEDLINE/PubMed was searched for the period 2015–2020 for english-language studies using the following key terms: infertility, depression, anxiety, assisted reproductive technology, infertility treatment. Open and randomized controlled trials, original observational studies, case reports, case series, and reviews were included. Initial search with key words returned n = 515 of which n = 467 did not match inclusion criteria: full text articles, female participants, age ≥18 years old. So, 48 articles were included into this literature review.

RESULTS

Causes of infertility

Fertility is affected by several factors: age, acute or chronic illness, environmental pollution, occupational factors, harmful habits, infectious diseases, genetic conditions, and specific reproductive disorders that can affect a man or woman trying to conceive.

According to a World Health Organization (WHO) study, of the 8,500 infertile couples studied in developed countries, found: female infertility, 37%; male infertility, 8%; both female and male infertility, 35%. The infertility of the remaining pairs was not elucidated or abstained during the fetal study [10]. A more detailed analysis highlights the following specific causes of infertility in women [11]: ovulation disorders – 25%, endometriosis – 15%, abdominal adhesions – 12%, tubal obstruction – 11%, other tubal lesions – 11%, unclear. Infertility of 10%, other causes – 9%, hyperprolactinemia – ≥ 7% [12].

Age is one of the most significant risk factors for infertility. It has been shown that a woman's chances of getting pregnant decrease with age. Not only is the number of oocytes decreasing, but the remaining oocytes are of poorer quality, which increases the incidence of chromosomal diseases and the likelihood of spontaneous abortions [13]. Women as they age also face an increased risk of developing disorders that lead to infertility, such as endometriosis, leiomyoma, or tubal disease [14]. Women undergoing oligo-ovulation or anovulation have difficulty becoming pregnant because the oocyte does not mature every month for fertilization. The most common cause of anovulation is polycystic ovary syndrome (POS) [15]. However, ovulation disorders can also occur for other reasons: hypothalamic-pituitary axis pathology, which can be caused by intense, inadequate exercise, eating disorders, hyperprolactinemia, autoimmune disease, etc. [16].

Mechanisms by which depression, anxiety, and emotional distress may contribute to infertility include hypothalamic – pituitary – adrenal (HPA) axis dysregulation [17], gonadotropin – releasing hormone (GnRH) pulse suppression [18], and autonomic nervous system activation [19]. Secondary effects of depression and anxiety on general health and diet can also lead to infertility. In addition, depression may reduce women's motivation to continue infertility treatment after treatment failure. Unfortunately, the evidence investigating the link between infertility and depression or anxiety is not complete. The meta-analysis done by Matthiesen et al. (2011) have found that stress and anxiety were associated with lower clinical pregnancy rates in women undergoing infertility treatment [20], but Boivin et al. (2011) meta-analysis have not found such association [21]. A large prospective study by Zaig et al. (2012) of women who underwent their first in vitro fertilization showed that the percentage of successful pregnancies was similar among women with or without mental symptoms or diagnoses [22].

Thus, depression can be not only the cause or consequence of infertility, but also as a consequence of failed infertility treatment.

Depression as a consequence of infertility

Is still unclear whether infertility is a consequence or cause of depression. Although the term "psychogenic infertility" is

being phased out, with all medically unexplained infertility attributed to psychological causes, many infertile women believe that the emotional stress they experience contributes to their continued infertility.

Infertility causes psychological, marital, and social phenomena of distress, including depression, stigma, sexual dysfunction, marital dissatisfaction, and withdrawal from family or friends [23]. Infertile patients often complain of stress and adaptation disorders, of which anxiety and depression are the most common [24]. Depression is a common reaction to infertility, often resulting from loss of identity, incompetence, or a sense of social stigma [25]. Infertility also particularly affects women, who are most often blamed for it [26] and affects many aspects of their lives, such as social, physical and psychological well-being [27]. In addition, a woman may lose a close relationship with her partner, a status in society, develop a low self-esteem, may lose hope for the future, and these feelings may lead to depression [28].

The ICD-10 classification identifies three main symptoms of depression: persistent sadness or low mood and / or loss of interests or pleasures and fatigue or low energy. The are also other seven associated symptoms but they are not main. These symptoms should last for at least 2 weeks [29].

Despite the high prevalence of infertility, infertile women do not share their infertility history with family or friends, thus increasing their psychological vulnerability. The inability to reproduce naturally can lead to feelings of shame, guilt and low self-esteem. These negative feelings can lead to varying degrees of depression, anxiety, suffering, and impaired quality of life [30].

The prevalence of depression among infertile women varies from 8% to 54%. Depression is considered to be one of the major health problems associated with infertility, especially in developing countries, where having a child is crucial for socio-cultural, economic, and religious reasons. Jasim et al. study found that depression was prevalent in 68.9% of the population in Iraq. Of women with depression, 42.2% had mild depression, 50.3%. – moderate depression, and only 7.5% – major depression. The analysis showed that the duration of infertility longer than 5 years was significantly associated with depression. Primary infertility was also found to be significantly associated with depression (95%). Other variables found such as duration of treatment and men's threat to another marriage were significantly associated with depression. All other variables studied did not show a significant association with depression [25]. Several studies have identified factors associated with depression and / or anxiety in infertile women. Domar et al. found that depression peaked in the third year after infertility diagnosis [31]. Matsubayashi et al. performed psychological tests on infertile women and healthy pregnant women. They found that infertile women had significantly higher psychological stress scores [32]. The study also found that anxiety and depression are caused by a lack of male support for an infertile woman [33]. In another Ramezanzadeh et al. study conducted in 2006 (n = 370), 86.8% of infertile women had symptoms of anxiety and 40.8% of women suffered from depression. An association between anxiety, depression and the duration of infertility has been identified with the greatest occurrence occurring 4 to 6 years after the diagnosis of infertility [34]. Another study in Vietnam involved 401 women. This study found that depression was more common in infertile women than in the general Vietnamese population [35]. However, this prevalence was lower than the prevalence of depression among infertile women in other populations, as found by Lok et al. [36], Fatemeh et al. [37] and Al Homaidan [38] (prevalence was 33%, 40.8%, and 53.8%, respectively).

Kanclerytė et al. conducted a study in Lithuania, which examined the emotional state of 107 infertile women. The results of the study showed that 68.6% of participants had symptoms of anxiety and 21% of women suffered from depression. Also there was no statistically significant ($p > 0.05$) difference in the prevalence of anxiety and depression according to age, marital status, co-morbidities and possession of harmful habits. However, although insignificant, the results show that anxiety was more pronounced in younger patients and depression more common occurred among older women. [39]

Thus, infertile women experience distress that includes social stress, depression, sexual dysfunction, and dissatisfaction with marriage [40]. However, it should be noted that psychological symptoms can be caused not only by the diagnosis of infertility but also by the failure of infertility treatment.

Depression as a consequence of infertility treatment

Recently, much attention has been paid to the relationship between infertility treatment using artificial insemination methods and the onset of mental disorders, most commonly anxiety and depression [41]. In 2011 Mariko Ogawa et al. conducted a study involving 83 Japanese women who were examined and treated for infertility at the Tokyo Reproduction Center at Ichikawa General Hospital College of Dentistry from February to April 2018. The psychological status of women was assessed by several tests: the Self-rating Depression Scale (SSD) and the Hospital Anxiety and Depression Scale (HADS). The results of the study revealed that patients treated for infertility had higher HADS depression scores compared to patients who were not treated [42]. Other studies have found that more than half of all infertile women describe infertility treatment as "the most stressful experience of their lives" [43, 44]. In women undergoing infertility treatment, major depressive disorder (MDD) is as high as 17% to 19.5% [45]. Medications used to treat infertility, including clomiphene, leuprolide, and gonadotropins, have also been linked to psychological symptoms such as anxiety, depression, and irritability. Therefore, going halfway through treatment, it is difficult to distinguish whether psychological symptoms are caused by infertility or whether it is a side effect of medication. The longer a patient is treated, the more often symptoms of depression and anxiety occur.

Nearly 40% of couples treated for infertility were still unable to conceive [46]. Patients who had one treatment failure had significantly more pronounced symptoms of anxiety and patients who experienced two failure had significantly more pronounced depressive symptoms compared with patients who did not receive infertility treatment [47]. Little Lund et al. study showed that 15% of women whose infertility treatment did not end in pregnancy suffered from major depression [45]. It has been found that distress can last up to 20 years after unsuccessful infertility treatment [48]. Patients undergoing

fertility treatment are at high risk for mental disorders, so it is important to recognize them in a time, help patients to deal with them and help them cope.

CONCLUSIONS

Depression is one of the major clinical problems faced by women diagnosed with infertility. As the duration of infertility increases, the incidence of depression increases. Ineffective treatment of infertility is one of the risk factors for the development of depressive disorder. It has been observed that patients with infertility have been diagnosed with a more severe degree of depression compared with women who have received specialized psychological care. Thus, infertile women should be counseled and supported throughout the treatment process, as psychological support for these women can prevent depression or reduce its symptoms.

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Received 27 August 2020, accepted 19 November 2020
Straipsnis gautas 2020-08-27, priimtas 2020-11-19