

# The Psychological Effects of Hormonal Treatment on Women Under IVF Treatment: A Comprehensive Review

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## ABSTRACT

This comprehensive review delves into the intricate world of assisted reproductive technologies (ART) and hormonal treatments, exploring their profound psychological effects on women undergoing IVF treatment. The psychological distress of infertility, combined with the demanding nature of ART, has been widely acknowledged, yet a comprehensive examination of the psychological impacts has remained elusive. This study examined the psychological repercussions of hormonal medications used in IVF, addressing the complex interplay of hormones and their effects in each stage of the IVF process. This review followed PRISMA guidelines and included studies from PubMed, Google Scholar, and ScienceDirect. A total of nine papers were collected. The findings of this study identified that depression, anxiety, mood swings, irritability, sleep disturbances, and cognitive changes were the most commonly seen medically induced psychological effects among the IVF patients. This review offers a holistic understanding of the psychological intricacies of IVF treatment, highlighting the imperative need for a more comprehensive approach to address the emotional wellbeing of individuals undergoing fertility procedures.

**Keywords:** Infertility, In Vitro Fertilisation, Psychological Distress, Women

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## INTRODUCTION

The experience of infertility may elicit psychological distress in both males and females, and it is widely recognised that the use of assisted reproductive technology (ART) treatment can impose substantial demands on individuals.<sup>1</sup> ART, including intrauterine inseminations (IUI), in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI), and third-party arrangements involving donated embryos, gametes, gestational carriers, or surrogates, have become increasingly utilised by a diverse range of individuals and couples who desire to achieve biological parenthood. This includes married or committed couples, gay or lesbian couples, as well as individuals who choose to become solo parents.

IVF is a popular and widely used way of treating infertility because of its alleged effectiveness. British researchers conceived their first child through IVF in 1978. 1% of all children born in the United States, roughly 2% in the United Kingdom, and over 4% in Finland and Denmark were conceived through IVF in 2010.<sup>2</sup> IVF is a multistep procedure comprising ovarian stimulation, ovulation induction, oocyte retrieval, fertilisation with sperm, and transport of the fertilised oocytes to the uterus for implantation and maturation. Each stage must be closely monitored by the administration of medicines. At each step, there are numerous protocols for the administration of these medications, and the most appropriate pharmacologic regimen and therapeutic intervention are determined after a complete pretreatment examination and an accurate diagnosis.<sup>3</sup>

Controlled ovarian stimulation is accomplished by employing the gonadotrophin-releasing hormone (GnRH) protocol and inhibitors of endogenous steroid hormones, including clomiphene citrate (CC), recombinant follicle-stimulating hormone (rFSH), and luteinizing hormone (LH).<sup>4</sup> A variety of fertility medications are employed throughout the IVF procedure, with certain medications administered orally while others are administered by injection. The specific type and dosage of drug used during IVF are contingent upon several factors, including the woman's age, test outcomes, and the stimulation regimen recommended by her physician. It is well known that IVF is an extremely tough process to go through mentally, despite being one of the most widely used ART techniques. According to research, the psyches of individuals going through IVF treatment deal with significant changes.<sup>5</sup> There exists an intricate relationship between infertility, psychological issues, and the treatment of infertility. Even though assisted reproductive technologies (ART) are becoming more common, there are no set guidelines for psychological and psychiatric processes for dealing with mental health issues that arise with the diagnosis and management of sterility.<sup>6</sup>

Numerous articles examined the psychological distress that infertile couples experienced as a result of psychosocial factors; however, treatment-specific or treatment-induced psychological distress received

the least attention. There has been a lack of research specifically focusing on the psychological distress that arises from the treatments used for infertility. Since the early days of IVF, optimising ART procedures to maximise efficacy and success of treatment have received attention<sup>7</sup>; nevertheless, psychological stress brought on by various ART treatment techniques has received less attention. While there has been research examining the impact of sex steroids on the neurological process in both genders, regardless of their mental diseases,<sup>8</sup> there is a lack of comprehensive reviews that have specifically investigated the effects of hormonal therapies for infertility on mental health in women. There exists a necessity for research pertaining to the psychological outcomes of hormonal intervention for infertility in women. Henceforth, the primary aim of this study was to examine the psychological reactions elicited by reproductive treatment and the drugs employed in the IVF technique. The main objectives of the research were twofold: 1) To identify psychological distress that is induced by medicines used in IVF. 2) To provide a comprehensive overview of the IVF procedure and its psychological consequences.

## METHODOLOGY

**Search Strategy:** An extensive literature study was conducted from September to December 2023. This review analysed publications published in the past 25 years. The literature search utilised specific keywords to locate studies that evaluated the psychological effects of hormone treatment on women undergoing IVF. The literature search was limited to publications written in the English language, specifically in Google Scholar, PubMed, and ScienceDirect. Relevant keywords were found, and MeSH terms were chosen prior to doing the search in the PubMed database. The pertinent keywords employed in the literature search were organised in Table 1 based on the databases. The Boolean operators "OR," "AND," and "NOT" were utilised to restrict the search to articles that address the relevant subjects. The asterisk was used to include all potential word ends. Additionally, a reference search of the selected articles was carried out to prevent any potential omissions of relevant literature. The selected studies, after removing duplicates, were then exported to an Excel file. Two reviewers scanned the records according to the PRISMA guidelines. (Table 1)

**Inclusion Criteria:** The search for this review was primarily focused on clinical trials, cross-sectional studies, and articles that evaluate the psychological effects and impact induced by hormonal treatment during the IVF process. Only studies published between the years 2000 and 2024, spanning a period of 25 years, were considered. The study included articles from different fields like reproductive medicine, psychology, pharmacology, and sociology. Peer-reviewed, full-text open access, and articles written in English across nations have been taken for review.

**Table 1: Keywords used for different databases to select the article**

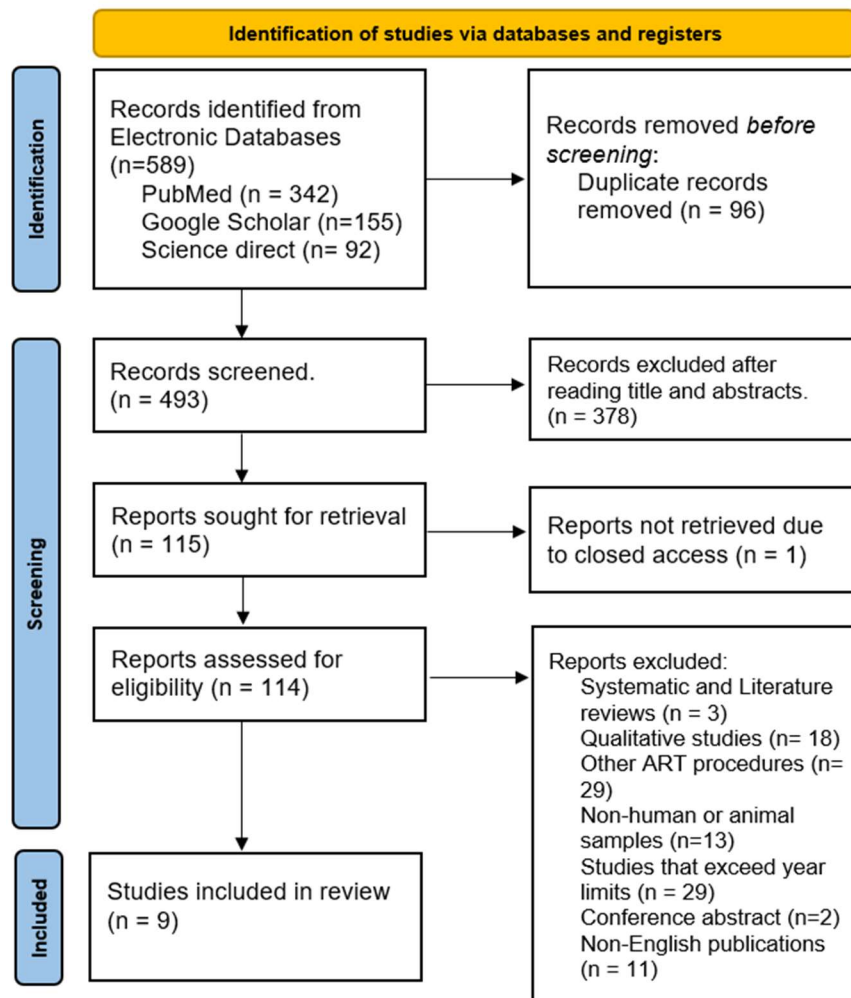
Database	Keywords used
Google Scholar	"Infertility" OR "treatment-induced psychological distress" OR "hormonal treatment" OR "IVF" OR "Medicinal effects" AND "women"
Pub-Med	"Invitro Fertilisation" OR "Birth control pills" OR "GnRH" OR "Lupron" OR "HMG" OR "HCG" OR "FSH" OR "ovarian stimulation" OR "oocyte retrieval" OR "psychological effects" OR "embryo transplant" OR "psychological impact of IVF procedure"
ScienceDirect	"Infertility" OR "Assisted Reproductive technology" OR "Psychological Consequences" OR "Hormonal treatment" OR "IVF" NOT "IUI" OR "ICSI" OR "Surrogacy"

**Exclusion Criteria:** Articles on other ART treatments and those not assessing the prevalence of treatment-related psychological symptoms among the infertile patients undergoing IVF were excluded. Conference proceedings, book reviews, and case series were not included.

**Approval of Institutional Ethical Committee:** Not applicable. However, this paper is a component of the author's PhD research. The Institutional Ethical Committee for Studies on Human Subjects (IECH) at Vellore Institute of Technology has approved (Ref. No. VIT/IECH/XIII/2022/04d) the intended doctorate research project.

**Data collection process:** A detailed review of the li-

terature was done between September and December 2023. A total of 589 items were found in the first search. Additionally, the references provided in these publications and abstracts were manually searched to discover other relevant articles. In accordance with inclusion and exclusion criteria, the authors removed duplicate or ineligible titles, abstracts, and complete texts. The authors completed the first round of full-text screening of the selected articles to determine the eligibility of the short-listed papers. The researchers followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines and came to a consensus on the final papers to be included in the review. The flow chart represents the selection process.



**Figure 1: displays the flow chart of the selection process**

**Quality of article:** Two reviewers reviewed data and evaluated the risk of bias and the quality of the research work using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) technique. GRADE evaluates the potential for bias, lack of accuracy, inconsistency, indirectness, and publishing bias. The authors conducted an extensive assessment of each article to determine the quality of the evidence and recommendations. Based on the evaluation, the articles selected for the study were assigned ratings of 'high', 'moderate', 'low', and 'very low' to indicate their quality and certainty. A total of nine original research papers were gathered. The quality assessment identified six studies as being of high quality.

The evidence's quality is graded as follows:

**High:** The authors are very certain that the actual effect is comparable to the estimated effect.

**Moderate:** The authors are confident that the actual impact is likely to be quite similar to the estimated impact.

**Low:** The actual impact is likely to be significantly different from the expected effect.

**Very Low:** The actual impact is likely to be very divergent from the estimated effect.<sup>9</sup>

## RESULTS

The obtained studies were tabulated, including the details of the authors, samples, country, study design, study process, chief findings, and quality of article.

**An et al.**<sup>12</sup> examined how psychological stress, hypothalamic pituitary adrenal axis modifications, and sympathetic nervous system changes impact reproductive outcomes during different stages of the first IVF cycle. The results of fluorometric and radioimmunoassay analyses revealed elevated levels of norepinephrine ( $p=0.03$ ) and cortisol ( $p=0.02$ ) in non-pregnant women after ovarian stimulation. Compared to pregnant women, non-pregnant women had higher cortisol levels at pregnancy detection day and following ovarian stimulation ( $t=4.8$ ;  $P<0.01$ ) and retrieval ( $t=2.6$ ;  $P=0.01$ ).

**Bloch et al.**<sup>13</sup> conducted a study where participants were randomly assigned to either short ( $n=60$ ) or long ( $n=48$ ) procedures to assess levels of depression and anxiety between the two groups. The process entailed the administration of 0.1 mg/d subcutaneous injections of GnRH-a triptorelin (Decapeptyl) for a duration of 14 days, followed by 225 IU of recombinant-FSH (r-FSH) (Gonal-F). In the short protocol, GnRH-a was delivered on the first day of the cycle, coupled with 225 IU of r-FSH daily. Choriogonadotropin alfa 250 mcg (Ovitrelle) was administered when three follicles attained 18 mm in diameter. Depression and anxiety symptoms showed an increase from the hypogonadal phase to the gonadotropin stimulation during IVF-ET cycles.

**de Klerk et al.**<sup>14</sup> aimed to examine whether using

mild ovarian stimulation in conjunction with single embryo transfer (SET) is a patient-friendly option compared to traditional in vitro fertilisation (IVF) treatment. However, there were no differences in physical pain between the two research groups during the subsequent treatment phases. Using modest ovarian stimulation and SET after the first IVF treatment cycle does not increase the prevalence of psychological symptoms compared to standard IVF. Due to the shorter length of mild stimulation protocols, patients experience physical and psychological symptoms for a shorter amount of time.

**Grigороva M. et al.**<sup>15</sup> reported that after four weeks of treatment, twenty-five women who were taking leuprolide acetate depot (LAD), a GnRH analogue that chemically suppresses ovarian function, showed a significant decline in mood, health-related symptoms, and performance on two WM tests. These findings present further evidence that oestrogen has a significant role in retaining working memory functions in women under reproductive medicine.

Research conducted by **Choi et al.**<sup>16</sup> found that 77.8% of women in the CC group and 94.8% of women in the HMG group reported experiencing psychological adverse effects while using reproductive medicines.

**Haemmerli Keller et al.**<sup>10</sup> investigated the effect of gonadotropin stimulation on psychological distress during IVF procedures. The researchers conducted an analysis on data collected from 57 individuals undergoing NC-IVF and 62 patients undergoing cIVF. Patients undergoing NC-IVF had a statistically significant decrease in depression levels (13.4 vs. 15.7,  $p<0.05$ ) and a greater degree of satisfaction with the treatment (67.9 vs. 62.9,  $p<0.05$ ) compared to patients undergoing cIVF. However, the actual factor influencing the psyche of women was not specified in this study. Another study by **Mamata et al.**<sup>11</sup> compared the GnRH antagonist protocol with the GnRH agonist protocol to determine the psychological and physiological burden. The study identified no substantial difference in psychological or physical burden between the two protocols. In contrast, the study by **Toftager et al.**<sup>2</sup> discovered that psychosocial and physical well-being were comparatively better in the GnRH antagonist protocol and worse in the GnRH agonist protocol. Women in the GnRH antagonist group reported lower levels of emotional distress (adjusted odds ratio [AOR] 0.69), less interference with their daily activities (AOR 0.74), fewer instances of unexpected grieving (AOR 0.71), and higher ratings for the quality of their sleep (AOR 1.55). In addition, women in the GnRH agonist group reported experiencing more severe physical discomfort. It is crucial to address the psychological stress that IVF treatments cause in order to improve patient outcomes.

**Yong, Martin, & Thong**<sup>17</sup> used gonadotropin injections (Metrodin HP or Gonal-F) and a gonadotropin-releasing hormone analogue (Buserelin or Nafarelin)

**Table 2: The psychological outcomes of medications and interventions in IVF treatment**

Authors	Samples	Country	Study design	Study Process	Chief findings	Quality
<b>Haemmerli-Keller et al. (2018)</b> <sup>10</sup>	Sample Size: 119 57 in the NC-IVF group and 62 in the cIVF group	Switzerland	Non-randomised controlled study	This paper compared two different IVF treatments: natural cycle IVF and conventional IVF (administration of gonadotrophin stimulation).	Patients undergoing cIVF experience greater psychological distress than those undergoing NC-IVF. The cIVF group had more depressive symptoms and a lower quality of life than the NC-IVF group.	Low <sup>a</sup>
<b>Toftager et al. (2018)</b> <sup>2</sup>	Sample Size: 1023 528 in the Short GnRH Antagonist Protocol and 495 in the Long GnRH Antagonist Protocol	Denmark	Randomised controlled trial	This paper compared the short and long GnRH antagonists.	Psychosocial and physical well-being were comparatively better in the GnRH antagonist protocol and worse in the GnRH agonist protocol.	High
<b>Mamata et al. (2015)</b> <sup>11</sup>	Sample size: 671  230 in GnRH antagonist and 441 in GnRH agonist	India	Nonrandomised controlled trial	This study conducted a comparison between the GnRH antagonist protocol and the GnRH agonist treatment to evaluate the physical and psychological strain associated with each protocol.	The study found no substantial difference between two groups on Physical or psychological burden.	Low <sup>a</sup>
<b>An et al. (2013)</b> <sup>12</sup>	Sample Size: 264 92 pregnant women and 172 non-pregnant women	China	Time series experimental research design	This study compared the anxiety, depression, cortisol, and norepinephrine levels at different stages of the IVF process between pregnant and non-pregnant women.	IVF treatment was associated with significant psychological and endocrinological differences before, during, and several weeks following the procedure. Norepinephrine and cortisol levels increased significantly during ovarian stimulation. Treatment efficacy was inversely associated with anxiety scores and favourably correlated with serum norepinephrine and cortisol.	High
<b>Bloch et al. (2011)</b> <sup>13</sup>	Sample size: 108 60 in the short GnRH agonist protocol and 48 in the long GnRH agonist protocol.	Israel	Time series experimental research design	The study compared two different controlled ovarian stimulation protocols: a "long protocol" inducing hypogonadism and a "short protocol" in which hypogonadism is not induced.	Both the long and short protocols had a significant impact on anxiety and depression, indicating a notable increase in symptoms, mostly observed from the hypogonadal phase to the follicular phase.	High
<b>de Klerk et al. (2006)</b> <sup>14</sup>	Sample size: 388 187 in the mild IVF group and 172 in the conventional IVF group	Netherlands	Randomised controlled trial	This study compared the psychological well-being of the women undergoing mild stimulation with single embryo transfer with conventional IVF.	Except for the day of oocyte retrieval, modest ovarian stimulation combined with single embryo transfers did not significantly affect psychological well-being compared to conventional IVF. Positive affect was lower and negative affect was greater in the mild IVF group.	High
<b>Grigorova, Sherwin, &amp; Tulandi (2006)</b> <sup>15</sup>	Sample Size: 50 25 in the leuprolide acetate group and 25 in healthy individuals	Canada	Randomised controlled trial	This study evaluated the influence of the sex steroid hormone leuprolide and compared it with that of healthy individuals.	There was a decline in verbal memory capacity, working memory, and a few functional deficits among females who were administered leuprolide acetate.	High
<b>Choi et al. (2005)</b> <sup>16</sup>	Sample Size: 454 162 in the CC group, 153 in the HMG group, and 139 in the control group	Canada	Cross sectional survey	This study assessed the patients under CC and HMG to evaluate the psychological side effects caused by these drugs.	Women under CC or HMG reported higher rates of psychological side effects than the control group, including irritability, restlessness, mood swings, feeling sad, and bloating. The HMG group scored higher than the CC group.	High
<b>Yong, Martin, &amp; Thong (2000)</b> <sup>17</sup>	Sample size: 37 women	United Kingdom	Longitudinal survey-based study	This study examined women's stress level during the extended protocol of controlled ovarian stimulation and completed the survey at the following points in time: (a) before receiving treatment, (b) before transferring embryos, and (c) before a pregnancy test.	Oocyte retrieval and pregnancy testing proved to be the most stressful stages of the IVF process.	Low <sup>b</sup>

<sup>a</sup>**Risk of bias-** A nonrandomized controlled trial (NRCT) was used for the study. Since the participants were not randomly assigned, there is a high chance of bias. The results may be subject to confounding and selection bias, both of which have the potential to compromise their validity.

<sup>b</sup>**Imprecision-** The study's sample size was comparatively small, which would have reduced the precision of the effect estimations.

for ovarian stimulation. The researchers examined the psychological functioning of the women at three time points using a self-reported Mean Affect Adjective Checklist. Results showed no significant changes in anxiety, sadness, and anger levels between pregnant and nonpregnant groups throughout all three visits. Visit 3 had substantially higher ratings for hostility, sadness, and anxiety compared to visits 1 and 2 ( $P \sim 0.001$ ). The anxiety levels for visits 2 and 3 were not substantially different. Visit 3 had lower positive affect ratings than visits 1 and 2, whereas visits 2 and 3 had lower sensation-seeking scores than visit 1.

## DISCUSSION

Psychological distress, such as anxiety, grief, and depression, appears to be more common in infertile people having assisted reproduction, especially if treatment has failed.<sup>18</sup> Research has observed that the emotional state of both men and women, particularly in terms of mood fluctuations such as anxiety, depression, or distress, varies during the treatment process. Specifically, depression and anxiety tend to rise on the day of oocyte collection, reduce on the day of embryo transfer, and increase again on the day of pregnancy testing. Furthermore, repeated cycles of treatment tend to decrease the intensity of emotional distress.<sup>19</sup> There have also been reports of acute mental episodes occurring at various IVF treatment phases.

A number of medications used to treat infertility affect neurotransmitter systems that regulate emotions. The first step in IVF is birth control. Birth control pills include oestrogen and progesterone, which prepare the ovaries for stimulation. This approach also helps control the menstrual cycle, plan and coordinate follicle growth, and prevent ovarian cysts.<sup>20</sup> However, birth control medications are not suitable for all individuals pursuing fertility treatment. Patients over 40 with high blood pressure, aura migraines, or other hemodynamic issues cannot receive BCPs.<sup>21</sup> If a patient cannot tolerate birth control tablets, norethisterone can regulate the menstrual cycle before fertility treatment.<sup>22</sup> Norethisterone is a synthetic form of progesterone. Progesterone plays a critical role in enhancing the uterine environment and supporting pregnancy maintenance.<sup>23</sup>

Progesterone in oral contraceptives has been proven to inhibit tryptophan oxygenase, and this decrease in tryptophan metabolism has been linked to depression.<sup>25</sup> An estimated 5% to 50% of women taking oral contraceptives experience depression, with progesterone-dominant tablets having the highest prevalence. Nevertheless, certain studies have documented the initiation of frequent mood shifts in women as a result of the oestrogen contained in oral contraceptive pills.<sup>26,24</sup>

The second step involved in IVF is ovarian stimulation (OS). OS is a crucial step in the IVF protocol, in-

volving the administration of drugs to stimulate the development of ovarian follicles. Gonadotropin hormone injections are commonly used to induce ovarian stimulation and promote oocyte production. These oocytes are then fertilized with sperm in a laboratory to create embryos for transfer into the uterus.<sup>27</sup> Initially, IVF used clomiphene citrate (CC), which has both anti-ovarian and estrogenic effects, for controlled ovarian stimulation (COS). CC acts on the hypothalamus by binding to oestrogen receptors for an extended period of time.<sup>28</sup> Researchers have identified aromatase inhibitors as viable alternatives to clomiphene citrate for inducing ovulation. During COS, combining gonadotropin with the aromatase inhibitor letrozole may reduce the total amount of gonadotropin needed for IVF.<sup>29</sup>

Human menopausal gonadotropins (HMG), including highly pure HMG and recombinant follicle-stimulating hormone (rFSH), have been used for COS.<sup>30</sup> Chapon et al. (2021) identified that rFSH was associated with a greater number of oocytes produced in comparison to HMG.<sup>31</sup> A study found that women using CC or HMG reported higher rates of psychological side effects, including irritability, restlessness, mood swings, feeling sad, and bloating.<sup>16</sup> Another study found that clomiphene induces mood instability in 60–70 percent of patients, with probable psychosis and manic delirium; however, more severe alterations were uncommon.<sup>32</sup>

GnRH agonists or antagonists will be given with FSH to prevent premature ovulation from LH increases. The triggering agent can be given using a standard, ultra-long, or short (flare) procedure depending on the patient's features and oocyte maturation GnRH agonist needs.<sup>33</sup> Clinically, GnRH agonists improve ovarian stimulation control and ovulation time.<sup>34,35</sup> Gonadotropin injection and sustained GnRH-agonist pituitary downregulation are the standard treatments. Several studies found that GnRH boosts follicular development, decreases cycle cancellation, increases implantation and fertilization,<sup>36,37,38</sup> and improves IVF results.<sup>39</sup>

Lupron, an injectable fertility drug, was often used during downregulation before IVF. Lupron functions as a GnRH agonist. GnRH agonists temporarily increase FSH and LH, which are inhibited to provide negative feedback. This decreases hormone synthesis and regulates ovulation. Patients must get daily Lupron injections during ovarian stimulation. The duration of Lupron administration to a patient may vary slightly depending on individual hormonal requirements. IVF patients often get Lupron shots for two weeks.<sup>40</sup> Previous studies have documented a notable decline in verbal memory capacity, working memory, and a few functional deficits among females administered leuprolide acetate (which begins on the second day and lasts for 12 to 13 days).<sup>15</sup>

The woman may experience more stress and restlessness during the extended GnRH agonist protocol compared to the short GnRH antagonist protocol.

The length of the treatment and the pituitary's downregulation before gonadotrophin stimulation due to postmenopausal estradiol levels led to adverse effects such as weight gain, muscle pain, migraines, and hot flashes.<sup>2,14</sup> Individuals receiving GnRH agonists have observed negative mood effects, such as sadness, anhedonia, fatigue, and anxiety, due to the induced hypogonadism during the process.<sup>18,13</sup>

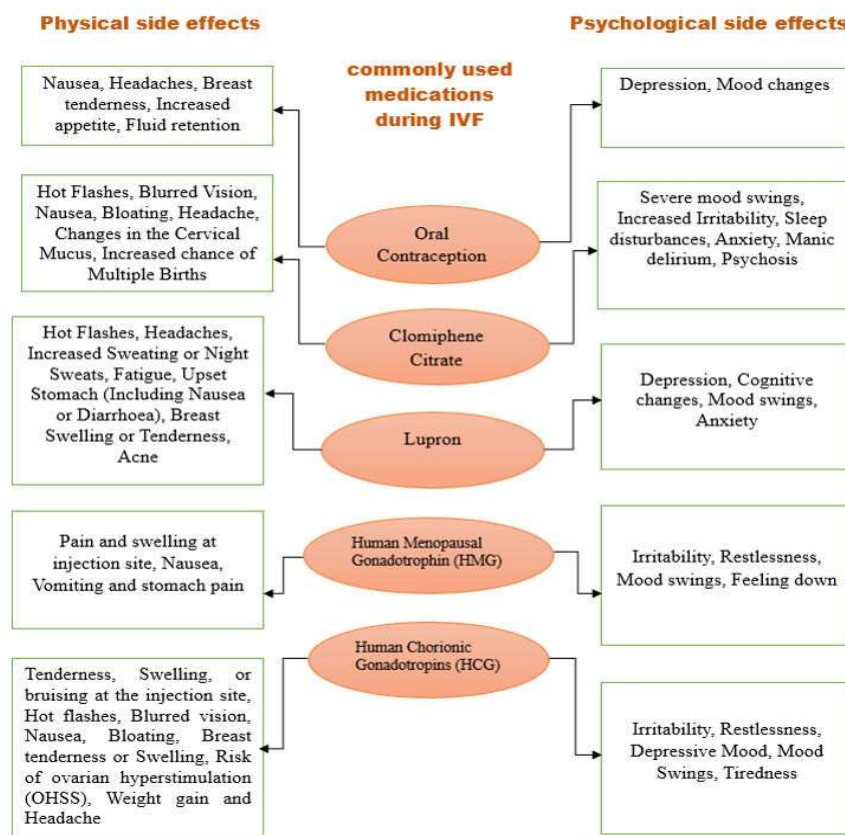
Cognitive issues, such as impaired concentration, memory, and fine motor coordination, have been reported by a number of women taking GnRH agonists. It is possible that these cognitive issues may or may not be concomitant with symptoms of mood disorders.<sup>41</sup> A study revealed that 44 percent of females under GnRH agonists claimed a reduction in perceived memory function, and memory returned to its baseline values when GnRH agonists were withdrawn.<sup>42</sup> Another study has examined the efficiency of long-acting s.c. goserelin with intranasally given buserelin acetate for pituitary down-regulation in 100 women undergoing ovarian stimulation for in vitro fertilisation. The results showed no significant difference in follicular development or clinical outcome between the two groups. However, higher incidents of fatigue, depressive symptoms, headaches, and abdominal pain among participants in the buserelin group in comparison with those in the goserelin group were observed, and no significant differences were identified in terms of mental irritability, nausea, and oedema.<sup>43</sup>

After ultrasonography and hormone levels indicated egg maturation, a "trigger shot" was given to com-

plete the process before egg retrieval. Human chorionic gonadotropin (HCG) stimulates follicle rupture and egg release in the "trigger shot." Administering the trigger injection around 36 hours before IVF oocyte retrieval is crucial for achieving a successful outcome of the IVF process. This injection contains one of these drugs: 1. Recombinant hCG (hCGr) injection, including Ovidrel; 2. Urinary-derived hCG (hCGu) shot, including Noravel, Pregnyl, and Profasi; 3. Agonist trigger shot, including Lupron, which surges LH release. Standard IVF trigger shots included 10,000 hCG units. Recombinant hCG, Ovidrel trigger shot, was recently used in 250 mcg dosages.<sup>45</sup>

The most common side effects of pregnyl and Ovidrel injections were irritability, depression, mood fluctuations, fatigue, weight gain, and headache. Bloating, discomfort, and pain in the abdominal or pelvic region may make patients more agitated and irritable.<sup>45</sup> Pain management approaches may help patients decrease such unpleasant effects and cope with the pain more effectively.

Pregnancy testing and oocyte retrieval have been identified as the most distressing stages of the IVF cycle.<sup>17</sup> Intriguingly, another study concluded that increased 5-hydroxytryptamine, renin, norepinephrine, angiotensin II, cortisol, and norepinephrine levels at the time of the pregnancy test have a detrimental effect on the outcome of the pregnancy.<sup>46</sup> This showed that the concentration of stress hormones has a negative impact on clinical pregnancy in IVF patients.



Source: self-made

**Figure 2: The physical and psychological side effects of commonly used drugs during IVF treatment**

The pharmaceuticals employed for the treatment of psychiatric disorders and infertility share unique properties as they are metabolized by the liver or impact the pituitary functions and hormones. Therefore, individuals with preexisting psychiatric disorders, currently on psychotropic medications, and undergoing fertility treatment require meticulous evaluation. In light of research findings, psychological symptoms may impede fertility, successful infertility treatment, and the capacity to tolerate ongoing treatment. Therefore, it is imperative that psychological symptoms be addressed to improve treatment outcomes and patient compliance.

## CONCLUSION

Based on a comprehensive review of the existing research, it can be inferred that the administration of drugs throughout the IVF procedure, as well as the procedure itself, elicits psychological changes in women receiving IVF. Depression, anxiety, mood swings, irritability, sleep disturbances, and cognitive changes were the most commonly seen medically induced psychological effects among the IVF patients.

## SUGGESTIONS & FUTURE DIRECTIONS

Not much research has been done on the psychological effects of IVF and its medications. Prospective studies should fill this research gap. Prior studies have predominantly concentrated on infertile women undergoing IVF therapy while neglecting the physical and mental well-being of infertile men and gestational carriers. Psychological interventions, such as couple counselling, psychoeducation, and fertility counselling, should be incorporated into the treatment protocol to reduce the implication of stress on IVF treatment outcomes. In addition to the infertile couple, donors and gestational carriers must be included in mental health considerations because they are also undergoing the distressing process of giving birth because of assisted reproduction. Policymakers must formulate essential policies to offer cost-effective treatment options for all individuals and to promote the well-being of infertile couples.

## ABBREVIATIONS

IVF	In Vitro Fertilization
IUI	Intrauterine Inseminations
ICSI	Intracytoplasmic Sperm Injection
GnRH	Gonadotropin-Releasing Hormone
COS	Controlled Ovarian Stimulation
LH	Luteinizing Hormone
FSH	Follicle-Stimulating Hormone
rFSH	Recombined Follicle-Stimulating Hormone
CC	Clomiphene Citrate
ART	Assisted Reproductive Technology
BCPs	Birth Control Pills
OS	Ovarian Stimulation
HCG	Human chorionic Gonadotropin
HMG	Human Menopausal Gonadotropins
WHO	World Health Organization
cIVF	conventional IVF

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