

**Section: Medical Science**

## **Major Depressive Disorder Association with Unsuccessful In-Vitro Fertilization (IVF) of Primary Infertile Women**

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**Abstract:**

**Background:** Women who go through unsuccessful IVF treatment were at increased risk of depressive disorders.

**Objective:** investigate the association between the unsuccessful IVF and depression among women with primary infertility.

**Methods:** a cross-sectional study included infertile women attending fertility center. Socio-demographic and clinical variables were compiled. Self-Reporting Questionnaire (SRQ-20) to identify mental illnesses; DSM-V criteria for depression and Hamilton-17 Scale for severity of depression, were used.

**Results:** high prevalence of depression among infertile women 80%. Unsuccessful IVF were 46%. About 26 % of infertile women with unsuccessful IVF were depressed. Depression was significantly associated with education, monthly income, duration of marriage, smoking, medication, chronic illness, and religion.

**Conclusion:** Depressive disorders are the most frequently observed disorder among infertile women exposed to unsuccessful IVF

**Keywords:** Depression; Primary Infertility; IVF; SRQ-20; DSM-V.

**Abbreviation:**

**IVF:** in-vitro fertilization,

**WHO:** World Health Organization,

**ART:** assisted reproductive technique,

**AID:** artificial insemination with the semen of a donor,

**AIH:** artificial insemination with the semen of the husband,

**ICSI:** intracytoplasmic sperm injection,

**PND:** postnatal depression, SRQ-20: self-rating questionnaire,

**HAM-17:** Hamilton depression scale-17,

**DSM-V:** diagnostic and statistical manual version five,

**BMI:** body mass index,

**SPSS:** Statistical package of social sciences.

## Introduction:

Infertility is a widespread condition known to affect more than 10% of all couples worldwide. It is regarded as psychologically stressful by most individuals and can lead to depression, social isolation and a lower quality of life<sup>1</sup>. The experience of having children is linked to every human life in the hope of a better, more beautiful and more productive tomorrow; and not having it is associated with a faceless state, mental confusion and frustration, especially among women<sup>2</sup>. The World Health Organization (WHO) defines infertility as not getting pregnant after a year of marriage without using a couple of contraception methods (quoted Mousavi et al., 2014)<sup>3</sup>. Reviewing several studies have shown that infertility is considered as a crisis with the potential to threaten the stability of individuals and has always been associated with a variety of psychological problems, such as anger, anxiety, stress, depression, obsession, decrease in sexual function and eventually, disappointment<sup>2</sup>. Most epidemiological studies report high intensity of anxiety and depression in people who participate in ART. However, due to the large methodological differences between the analyzed studies the results were very different. A number of studies identify an increased incidence of depressive symptoms in patients treated for infertility<sup>4</sup>. Such a conclusion was also confirmed in a critical analysis of previous studies conducted by Williams et al. who found that for women taking the therapy for infertility an increased incidence of depressive symptoms and major depression are observed<sup>5</sup>. Over the last years, impressive progress has been made in the development of medical technological interventions for fertility problems. Depending on the precise nature of the fertility problem, various reproductive technologies are available to help couples achieve a pregnancy. This includes in vitro fertilization (IVF), artificial insemination with the semen of a donor (AID), artificial insemination with the semen of the husband (AIH) and intracytoplasmic sperm injection (ICSI)<sup>6</sup>. It is reported that about 13% of women in developed countries suffer from postnatal depression (PND)<sup>7,8</sup>. Studies have shown that the prevalence of PND cases that require psychiatric care is 0.3%<sup>9</sup> and that the prevalence of hospitalizations due to PND is 0.06%-0.26%<sup>10</sup>. In general, women who undergo infertility treatment have fewer risk factors of PND. Ross et al. (2011) speculated that future studies controlling for these factors may in fact find the risk of PND to be increased among women who have undergone infertility treatment<sup>11</sup>. Since an increasing number of couples use IVF treatment to conceive<sup>12</sup> it is important to determine if this treatment increases the risk of PND<sup>13-15</sup>. Studies examining risk of psychiatric illness after IVF treatment have varied in their results. Baldur-Felskov et al<sup>16</sup> found that women who go through unsuccessful IVF treatment were at increased risk of hospitalization due to most psychiatric disorders<sup>16</sup>. Yli-Kuha et al<sup>17</sup> showed that the risk of depression was increased in those who had gone through an unsuccessful IVF treatment. Many studies focus on psychological issues within the context of in vitro fertilization (IVF), including the psychological states before, during and after the IVF treatment<sup>17</sup>. This study was done to investigate the association between the unsuccessful IVF and depression among women with primary infertility.

## Patients and Methods:

*Design and setting:* This is a cross-sectional study conducted on primary infertile women attending, Imamain Kadhmain Medical City, Um Al- Baneen fertility center, Baghdad, Iraq. Data collected during the period March, 1st, 2014 to September, 1st, 2017. *Study Population and Sampling Technique:* The study included women attending the fertility center during the data collection time. A systematic random sampling technique was applied. *Inclusion criteria:* all women with primary infertility of any age who welcomed participation were included. *Exclusion criteria:* Women with history of inability to conceive of less than 12 months, current serious or unstable medical illnesses that cannot complete the interview, not cooperative, and who did not give their consent to participate were excluded from the study. *Data collection Tools:* sociodemographic variables and clinical characteristics of women were compiled using a questionnaire filled through a direct interview. List contained question about exposures to in-vitro fertilization (IVF) failure. Mental status was assessed using

the SRQ-20 scale (self-reporting questionnaires) that was developed by the WHO and used in many countries<sup>18</sup>. Women with positive results were assessed for the presence of depression using the DSM-V criteria of depression<sup>19</sup>. Women with “depression” were further assessed for the severity of depression using the Hamilton scale<sup>20</sup>. *Definition of variables:* The independent variables evaluated to explain depression were socio demographics (age, education, occupation, and religious status), smoking habits, and duration of marriage. *Statistical Analysis:* Statistical package of social sciences (SPSS) version 20 was used for data entry and analysis. Categorical variables were tested using chi square test.  $P < 0.05$  was considered statistically significant. *Ethical Issue:* Official approvals were granted from the officials in the study setting. Informed consent was obtained from each participant to be included in this study. Names were kept anonymous and interviews were conducted with full privacy.

**Results:**

Total women with primary infertility approached were 320; age 17-42 ( $28 \pm 7$ ), Almost 77% of the women were aged below 35 years. Monthly income was 150000-150000000 Iraqi dinars ( $596000 \pm 326000$ ), Almost 95% of women from low and middle monthly income. Duration of marriage 1-20 years ( $7 \pm 4.5$ ), 85% were below 10 years (Table 1).

Nearly half of women were of low education. Employed women about 4% and all other were house wives. Smoker women were 7.5%. About 94% were taking different medication. Nearly half of women were mild religious (Table 2).

Infertile women with failure of trail of *invitro fertilization* were 148 (46.25%). More than half of them were depressed 84 (26.25%). This finding was statistically significant ( $P < 0.001$ ). (Table 3)

Infertile women with trial failure of IVF were of statistical significant correlation with age group ( $P=0.013$ ), education ( $P=0.013$ ), occupation ( $P=0.001$ ), monthly income of the family ( $P < 0.001$ ), the body mass index ( $P < 0.001$ ), the duration of infertility ( $P < 0.001$ ), and religion ( $P=0.015$ ). (Table 4)

Depression of infertile women was significantly associated with; education ( $P < 0.001$ ), monthly income of the family ( $P=0.005$ ), smoking habit ( $P < 0.001$ ), duration of infertility ( $P < 0.001$ ), medication history ( $P=0.021$ ), chronic illness ( $P=0.021$ ), and the body mass index ( $P < 0.001$ ). (Table 2)

Infertile women with SRQ-20 positive results were 256 (80%). Women met the DSM-V criteria of depression were 256 (80%). According to Hamilton scale, the severity of depression of infertile women was; mild 58 (18.1%), moderate 40 (12.5%), severe 82 (25.6%), and very severe depression 76 (23.8%). (Table 5)

The correlation trail of IVF of infertile women with SRQ-20 results, DSM-V criteria of depression, and the Hamilton severity of depression were strongly statistical significant results ( $P < 0.001$ ) (Table 5)

**Table 1: Range, Mean, and Standard Deviation of Primary Infertile Women Characteristics**

	Minimum	Maximum	Mean	Std. Deviation
Age	17.00	42.00	28.0937	7.70929
Income monthly	150000.00	1500000.00	596875.00	326455.62618
BMI	17.72	36.33	27.4060	4.80522
Marriage duration	1.00	20.00	6.9119	4.52232

**Table 2: Sociodemographic and Clinical Variables Correlate with Depression of Primary Infertile Women**

		DSM		Total (320)	%	P value
		NEGATIVE	POSITIVE			
Age Group	16-25 yrs	22	116	138	43.1	<b>0.062</b>
	26-35 yrs	30	80	110	34.4	
	36-45 yrs	12	60	72	22.5	
Education	illiterate	10	20	30	9.8	<b>0.000</b>
	primary school	22	96	118	36.8	
	intermediate school	12	42	54	16.8	
	secondary school	10	0	10	3.1	
	institute	10	56	66	20.6	
	college	0	42	42	13.1	
INCOME	> 500000 dinar	22	130	152	47.5	<b>0.005</b>
	500000 - 1000000 dinar	42	114	156	48.8	
	> 1000000 dinar	0	12	12	3.7	
occupation	employed	0	12	12	3.7	<b>0.077</b>
	house wife	64	244	308	96.3	
Smoking	No	52	244	296	92.5	<b>0.000</b>
	yes	12	12	24	7.5	
Marriage Durations	< 5 years	10	140	150	46.9	<b>0.000</b>
	5 - 10 years	42	82	124	38.7	
	> 10 years	12	34	46	14.4	
Medication	No	0	20	20	6.2	<b>0.021</b>
	Yes	64	236	300	93.8	
Chronic illness	no	64	236	300	93.8	<b>0.021</b>
	yes	0	20	20	6.2	
BMI	BMI < 25	34	124	158	49.4	<b>0.000</b>
	BMI 25-30	0	50	50	15.6	
	BMI > 30	30	82	112	35	
Total		64 (20%)	256 (80%)	320	100	

**Table 3: Correlation of Unsuccessful IVF with Depression**

	Non Depressed	Depressed	Total	P Value
Without IVF	0	172 (53.75%)	172 (53.75%)	<b>0.000</b>
With IVF	64 (20%)	84 (26.25%)	148 (46.25%)	
Total	64 (20%)	256 (80%)	320 (100%)	

**Table 4: Correlation of Sociodemographic and Clinical Variable of Infertile Women with Unsuccessful Trail Of IVF**

		IVF		Total	P value
		no	yes		
Age Group	16-25 years	86	52	138	0.013
	26-35 years	56	54	110	
	36-45 years	30	42	72	
education	Illiterate	20	10	30	0.013
	primary school	64	54	118	
	intermediate school	32	22	54	
	secondary school	0	10	10	
	Institute	34	32	66	
	College	22	20	42	
Occupation	employed	12	0	12	0.001
	house wife	160	148	308	
INCOME	> 500000 dinar	100	52	152	0.000
	500000 - 1000000 dinar	60	96	156	
	> 1000000 dinar	12	0	12	
BMI	BMI < 25	100	58	158	0.000
	BMI 25-30	40	10	50	
	BMI > 30	32	80	112	
Marriage Durations	< 5 years	110	40	150	0.000
	5 - 10 years	52	72	124	
	> 10 years	10	36	46	
Smoking	No	160	136	296	0.702
	Yes	12	12	24	
Chronic illness	No	162	138	300	0.728
	Yes	10	10	20	
Religion	Nil	46	22	68	0.015
	Mild	32	20	52	
	moderate	64	76	140	
	Severe	30	30	60	
Total		172	148	320	

**Table 5: Correlation of Depression with Unsuccessful IVF of Primary Infertile Women**

		IVF		Total	%	P value
		no	yes			
SRQ_20	NEGATIVE	0	64	64	20	0.000
	POSITIVE	172	84	256	80	
DSM-V	NEGATIVE	0	64	64	20	0.000
	POSITIVE	172	84	256	80	
DEGREE OF depression	no depression	0	64	64	20	0.000
	mild depression	38	20	58	18.1	
	moderate depression	40	0	40	12.5	
	severe depression	36	46	82	25.6	
	very severe depression	58	18	76	23.8	
Total		172 (53.75%)	148 (46.25%)	320	100	

**Discussion:**

The correlation of unsuccessful IVF of infertile women with SRQ-20 results, DSM-V criteria of depression, and the Hamilton severity of depression were strongly statistical significant results ( $P < 0.001$ ). Infertile women with unsuccessful *invitro fertilization* were 148 (46.25%). More than half of them were depressed 84 (26.25%). This finding was statistically significant ( $P < 0.001$ ). Study found 80% of infertile women were depressed. High prevalence of infertile women depression might be explained by that; in our culture, female always blamed for causes of infertility. Gynecologists are hurry to attribute couple infertility to female factors. Infertile women suffer social pressure from their relatives and friend. Unsuccessful IVF constitutes a crisis and stigma in affected women, may become isolated and neglected. The unsuccessful IVF reactions may include; frustration, shock, anger, depression, and grief, loss of self-esteem, self-confidence. Chen et al. 2004<sup>21</sup> found Psychiatric disorders were present in 40.2% of patients; 23.2% – generalized anxiety disorder; 17% – major depressive disorder; dysthymic disorder in 9.8% of patients<sup>21</sup>. Petersen et al. 2014<sup>22</sup>: Severe depressive symptoms were reported in 11.6% of women and 4.3% of men, and were significantly associated with increased infertility-related distress at the individual and partner level<sup>22</sup>. Current study found depression of primary infertile women was significantly associated with; education, monthly income, duration of marriage, smoking, medication, chronic illness, religion, and BMI. This association might be explained by the fact that the longer the infertility crisis continues, the more people in families and neighbors will know about it lead to more social pressure women will feel; another possible explanation is that longer infertility duration and repeated referrals would gradually change infertility to a chronic problem. Current study Findings was lower than the results of a study conducted in Pakistan<sup>23</sup> which showed depression was 95% in infertile women. Findings of current study were higher than many studies. The study done in Morocco<sup>24</sup> showed that 55% of the women had depression with positive relation to occupation. Nigerian study<sup>25</sup> depression was 54.5% of infertile women. Iranian study in Tehran<sup>26</sup> found 30.5 % of infertile women had depression with significant association to infertility duration and failure in previous treatment. Survey carried in Katowice, Poland<sup>27</sup> found

(22.52%) of women had light severity of depression. Chinese study in Guangdong Province<sup>28</sup> showed depression was 47.0% of infertile females. Nigerian study in Ogbomoso<sup>29</sup> found a prevalence of infertile female depression of 52.7%, with no significant association between the age group, level of education, duration of marriage, type of infertility. Indian study<sup>30</sup> showed depression in 41% of the infertile females which was correlated with duration of infertility, positive related to occupation and duration of infertility. Prevalence of depression among infertile women of current study was higher than many studies. Drosdzol (2009): 35.4%<sup>31</sup>. Farzadi (2008): 72.54%<sup>32</sup>. Ramezanzadeh (2004): 40.8%<sup>33</sup>. Haririan (2010):58%<sup>34</sup>. Peyvandi (2010): 62%<sup>35</sup>.

**Conclusion:** In patients treated with IVF for infertility mental disorders represent very common clinical problem. Depressive disorders are the most frequently observed disorder. Unsuccessful IVF constitutes an independent risk factor for development of mental disorders. Current study found high prevalence of depression among infertile women 80%. Unsuccessful IVF were 46%. About 26 % of infertile women with unsuccessful IVF were depressed. Depression was significantly associated with education, monthly income, duration of marriage, smoking, medication, chronic illness, and religion.

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**Conflict of interest:** The authors declare no conflicts of interest

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