DEPRESSION, ANXIETY AND SELF-ESTEEM AMONG INFERTILE WOMEN: A SYSTEMATIC REVIEW OF LITERATURE

VANESA NEGOIŢĂ1* and ADRIANA BĂBAN1

ABSTRACT. This paper aims to analyze the current literature on the impact of infertility on women's psychological health through systematic methods. A systematic review of the literature for the research of the psychological effects on infertile women was performed. Depression, anxiety and self-esteem were analyzed in the context of women with reproductive problems. Our results indicate that infertile women had higher levels of anxiety and depression, but also a lower self-esteem, compared to women without fertility problems. Almost half of the infertile women, presented in the literature included in this study, reported the presence of psychological problems. The risk factors identified as having important influences on the experience of infertility were age, level of education, employment, duration of infertility, type of infertility, known or unknown cause of infertility, intentionality, perceived social support and treatment for infertility. Of course, these experiences differ from woman to woman, but most of the times, the lifestyle and physical and mental health of infertile women are negatively affected.

Keywords: systematic review, female infertility, depression, anxiety, self-esteem.

ABSTRAKT. Ziel dieses Papier ist es, die aktuelle Literatur zu den Auswirkungen von Unfruchtbarkeit auf die psychische Gesundheit von Frauen durch systematische Methoden zu analysieren. Eine systematische Überprüfung der Literatur zur Untersuchung der psychologischen

_

¹ Department of Psychology, Babes-Bolyai University, Cluj-Napoca, Romania

^{*} Corresponding author: vanesa.98.vanesa@gmail.com

Auswirkungen auf unfruchtbare Frauen durchgeführt. Depressionen, Angstzustände und Selbstwertgefühl wurden im Kontext von Frauen mit Fortpflanzungsproblemen analysiert. Unsere Ergebnisse zeigen, dass unfruchtbare Frauen ein höheres Maß an Angstzuständen und Depressionen, aber auch ein geringeres Selbstwertgefühl hatten als Frauen ohne Fruchtbarkeitsprobleme. Fast die Hälfte der unfruchtbaren Frauen, die in der in dieser Studie enthaltenen Literatur vorgestellt wurden, berichten über psychische Probleme. Die Risikofaktoren, die einen wichtigen Einfluss auf Unfruchtbarkeit haben sind: Alter, Ausbildung, Beschäftigung, Dauer der Unfruchtbarkeit, Typ der Unfruchtbarkeit, bekannte oder unbekannte Ursachen für Unfruchtbarkeit. Absichtlichkeit. wahrgenommene soziale Unterstützung und Behandlung von Unfruchtbarkeit. Natürlich unterscheiden sich diese Erfahrungen von Frau zu Frau, aber in den meisten Fällen werden der Lebensstil sowie die körperliche und geistige Gesundheit unfruchtbarer Frauen negativ beeinflusst.

Schlüsselworte: systematische Überprüfung, weibliche Unfruchtbarkeit, Depression, Angst, Selbstwertgefühl.

INTRODUCTION

Infertility is defined as a disease of the reproductive system that is characterized by the inability to procreate after twelve months of regular sexual contact without the use of contraception (Zegers et al., 2009). Infertility is an increasingly common condition. According to the WHO, one in four couples in developed countries suffers from infertility (Global prevalence of infertility, 2014) and this number will increase probably with the increasing of the average age of women who become pregnant for the first time (Wilkins et al., 2010).

Infertility can function as a painful emotional experience (Dural et al., 2016). The most common psychological problems identified in previous research are high stress, depression anxiety, low self-esteem, sexual satisfaction problems, low quality of couple life (Ali et al., 2015; Allan, 2013; Carreño-Meléndez et al., 2011; Cousineau & Domar, 2007). Infertile women may also experience a relatively high level of frustration and anger because of prejudices in society against childless women.

In today's society, the definition of woman is still closely linked to the concepts of wife and mother, although in the last decades, the ideals of femininity have undergone a great transformation so that youth, beauty, fertility and love are also fundamental values (Cunningham, 2013; Díaz Bernal, & García Jordá, 2011; Moore, 1991). Depending on the beliefs that each woman has about her role as a woman and as a mother, the diagnosis of infertility can cause emotional disorders (Sañudo Toca, 2014). However, the results in the existing literature show some discrepancies in the associations between psychological consequences and female infertility.

The results in the existing literature show some discrepancies in the associations between psychological consequences and female infertility. Due to the great diversity of existing studies, many of them have a low methodological quality, do not correctly conceptualize the investigated problem, or do not take into account the factors that could mediate the analyzed associations. Several systematic reviews have been identified for the study of quality of life, psychological well-being, marital satisfaction and all these effects have been analyzed on both partners in a comparative model (Chachamovich et al., 2010; Luk & Loke, 2015). Other systematic reviews have been performed on the effectiveness of treatments for infertility or on the psychological effects of infertility caused by endometriosis or Polycystic Ovary Syndrome (Barry, Kuczmierczyk, & Hardiman, 2011; Frederiksen, Farver-Vestergaard, Skovgård, Ingerslev, & Zachariae, 2015; Pope, Sharma, Sharma, & Mazmanian, 2015). No systematic review has been published to investigate the psychological impact of infertility on infertile women. Moreover, there is not much research, let alone systematic reviews, to study the problems of depression, anxiety and self-esteem in an integrative form of these consequences.

Therefore, this study aims to systematically analyze studies that address the psychological problems of depression, anxiety and self-esteem among infertile women who are part of several cultures. In order to provide a realistic vision and a more complete understanding of this phenomenon, the risk factors that could influence the experience of women with reproductive problems will be considered and analyzed in an integrative and comparative way. This approach allows for an indepth exploration of the impact of infertility on today's women.

METHODS

This study is a systematic analysis of the literature published in the last 15 years, on the psychological impact of infertility on women. Given the systematic and critical nature of this paper, all procedures were performed in a rigorous manner, following all criteria in terms of the search and selection of studies and interpretation of results. The working procedure addressed in this research will be presented below.

Search strategy

This review analyzes studies focusing on infertile women of reproductive age, regardless of their marital status, living in any part of the world. Therefore, studies focusing on infertile men were excluded from this review. The cause of infertility, the type of infertility (primary or secondary), previous pregnancies, the duration of infertility and the age of the infertile women are not an exclusion criteria. Only those comparative studies between infertile men and infertile women that place great emphasis on the female experience were included, so that it is possible to extract significant results for this study.

At the same time, this study focuses on the experiences of women with infertility, more precisely, the psychological consequences on them. Studies that examine at least one of the following psychological consequences have been included: depression, anxiety and/or self-esteem. Therefore, any article that does not contain these consequences has been excluded.

Both qualitative and quantitative studies investigating the experiences of women with infertility (psychological consequences) were considered. Only studies published between 2004 and 2019, full-text, and those in English were included in this review.

The search strategy located exclusively published studies and included three stages. First stage started with a search in the electronic databases PubMed and PsycInfo and on Google Scholar, followed by an analysis of the words included in the title and abstract and the indexed terms used to describe the articles. A second search in the electronic databases PubMed, PsycInfo and Google Scholar using the identified keywords and index terms was performed in all included databases.

Finally, the list of referenced articles of all studies has been analyzed for further studies. Articles published from 2004 to 2019 were introduced in the research.

At the end of the systematic search, all identified citations were collected and uploaded to the EndNote reference management software, duplicate items were removed. Studies that met the inclusion criteria were accessed in full-text. The full text of the selected studies was taken over and evaluated in detail based on the inclusion criteria. If complete but inaccessible studies were identified, those articles were excluded from the analysis. Full-text studies that did not meet the eligibility criteria were excluded and the reasons for exclusion were recorded in an Excel document. The included studies underwent a critical evaluation process.

The data were extracted using Microsoft Excel. All studies included in the review were analyzed in detail. The most important data were the research methods, tools used, sample size, groups included, study location (country), year of publication, data on the psychological consequences of infertility (depression, anxiety and/or self-esteem) and risk factors.

Data synthesis

All data extracted from the articles included in this systematic review were subjected to critical and comparative analyzes to determine which are the risk factors, which information is common but also which are in opposition. In order to perform a critical and transparent analysis, all the details and possible explanations present in each study were taken into account. In the synthesis of the data, the cultures of the women surveyed and the tools used to make it possible to understand the discrepancies were taken into account.

RESULTS

After the first stage of searching in the electronic databases: PsycInfo and PubMed but also on Google Scholar, the following words were identified: infertility, women, psychological impact, psychological consequences, depression, anxiety, self-esteem, distress and infertility treatment.

Once the essential terms for searching the literature to be analyzed according to the inclusion criteria were established, 1177 articles were obtained from the databases used (745 from PsycInfo and 432 from PubMed) and 54 articles from the manual searches on Google scholar. Subsequently, based on the verification of the references in the articles found in the electronic databased, two more studies with probability of eligibility were obtained. Duplicates were eliminated (585 studies). Following the process of screening the title and abstract of the 648 studies, only 152 researches met the inclusion criteria. Finally, 17 studies were included, eight of them from PsycInfo, 5 from PubMed, 2 from Google Scholar and 2 from the references of other articles. The results of the literature search strategy can also be seen in Figure 1.

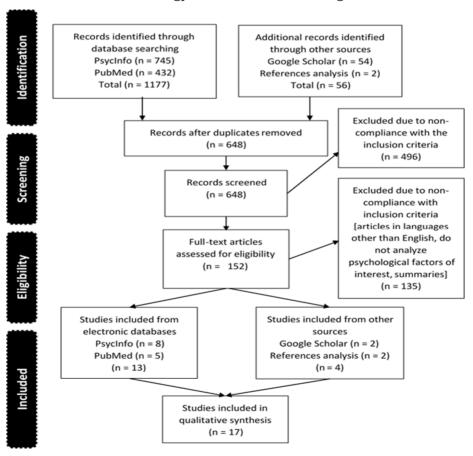


Figure 1. PRISMA flow chart for study selection.

Articles that predominantly analyzed male infertility (n=4), did not study at least one of the three psychological consequences – depression, anxiety and self-esteem (n=48), the full-text of the article was not found (n=40), were published in a language other than English (n=19) and were published before 2004 (n=24) were excluded.

Characteristics of selected studies

All 17 studies included in this analysis were published in journals. These are 15 quantitative studies, of which seven cross-sectional studies, a "case-control" study, two qualitative studies are included. Table 2 present the included articles and the types of studies.

The identified studies represent a diverse population of 13 countries, with 5 studies conducted in Europe (Germany, Italy, Poland and Portugal), 9 studies in Asia (India, Iran, Japan, Pakistan and Turkey), 1 study in Africa (Ghana), 1 study in South America (Chile) and 1 study in the USA (Table 2).

The total number of participants presented in these studies is 3799. The sample size ranged from 14 to 1027. The samples were represented and divided into various forms: (1) infertile women and fertile women; (2) infertile women and infertile men; (3) women with primary infertility and women with secondary infertility; (4) infertile women undergoing treatment for infertility and women without treatment; (5) infertile women undergoing treatment for infertility; (6) infertile women after a failed treatment; (7) infertile women without treatment (Table 2).

The literature focused on the three aspects of psychological effect on infertile women: depression, anxiety and self-esteem. Of the 17 articles included in this paper, three of them analyze a single psychological effect (depression or anxiety), two of psychological effects are studied in 13 studies (depression and anxiety, depression and self-esteem, anxiety and self-esteem) and only two studies analyze all three psychological effects (Table 1).

Reference Depression Anxiety Self-esteem Begum & Hasan (2014) Contreras, Jara & Vidal (2016) Donkor, Naab & Kussiwaah (2017) Drosdzol & Skrzypulec (2009) Facchin, Buggio, Dridi & Vercellini (2019) Farzadi & Ghasemzadeh (2008) Galhardo, Alves, Moura-Ramos & Cunha (2019) Greil, Shreffler, Schmidt & McQuillan (2011) Hasanpoor-Azghdy, Simbar & Vedadhir (2014) Kahyaoglu & Balkanli (2015) Maroufizadeh, Karimi, Vesali & Samani (2015) Massarotti et al. (2019) Ogawa, Takamatsu & Horiguchi (2011) Ramezanzadeh et al. (2004) Shahraki, Ghajarzadeh & Ganjali (2019) Tan et al. (2008) Verma et al. (2015)

Table 1. Psychological effects approached in the literature

Qualitative analysis of results from the literature

After the studies to be included in this paper were established, a comprehensive and in-depth analysis was performed to extract the relevant data, which were then entered into a table. Other important data such as the authors of each research, the year of publication, the sample size and the methods used were presented in Table 2.

Some differences have been identified in the results of the studies but what all the studies had in common is the statement that infertility does have a very large impact on women's mental health (Begum & Hasan, 2014; Contreras et al., 2016; Donkor et al., 2017; Drosdzol & Skrzypulec, 2009; Facchin et al., 2019; Fazardi & Ghasemzadeh, 2008; Galhardo et al., 2019; Greil et al., 2011; Hasanpoor-Azghdy et al., 2014; Kahyaoglu & Balkanli, 2015; Maroufizadeh et al., 2015; Massarotti et al., 2019; Ogawa et al., 2011; Ramezanzadeh et al., 2004; Shahraki et al., 2019; Tan et al., 2008; Verma et al., 2015). No article had contradictory findings.

Table 2. Summary of results from included studies

Reference	Year	Sample	Method	Results / Conclusions
Begum & Hasan (2014) Pakistan (Asia)	2014	n = 120 of which 60 infertile women without treatment and 60 fertile women.	Questionnaires. Comparative quantitative study.	Assigning guilt and responsibility for fertility problems are some of the factors that contribute to the development of depression and anxiety in infertile women. Another important factor is the lack of support from the family and the husband.
Contreras-Garcia, Jara-Riquelme & Manriquez-Vidal (2016) Chile (South America)	2016	n = 40 primary infertility women undergoing IVF treatment.	Questionnaires. Pilot study.	Blaming for treatment failure, lack of support from others contributes to lower self-esteem and creates symptoms of anxiety. Lack of hope can affect treatment outcomes.
Donkor, Naab & Kussiwaah (2017) Ghana (Africa)	2017	n = 14 women under treatment.		The passage of time without the possibility of conceiving, the observation of friends who have managed to conceive a child, the fear of losing their husband are some of the key elements for the development of depressive and anxiety symptoms.
Drosdzol & Skrzypulec (2009) Poland (Europe)	2009	n = 584 of which 206 infertile women without treatment.	Questionnaires. Cross-sectional quantitative study.	Risk factors for depression and anxiety include female gender, age over 30, lower level of education, lack of professional activity and duration of infertility of 3-6 years.
Facchin, Buggio, Dridi & Vercellini (2019) Italy (Europe)	2019	n = 127 infertile women, most without treatment.	Questionnaires. Quantitative study.	Infertile women who believe that women without children are less appreciated by others have reported higher levels of depressive symptoms and lower self-esteem. Shame is a direct predictor of depression.
Farzadi & Ghasemzadeh (2008) Asia	2008	n = 193 infertile women under treatment.	Interviews and questionnaires. Cross-sectional quantitative study.	Irrational cognitions of parents and pressure from relatives were the two main independent predictors of depression among infertile women. The duration of infertility is not associated with depression.
Galhardo, Alves, Moura-Ramos & Cunha (2019) Portugal (Europe)	2019	n = 124 infertile women under treatment.	Self-report and evaluation questionnaires. Cross-sectional quantitative study.	Representations about the importance of motherhood are indirectly associated with depressive symptoms, throughout the association with the impact of infertility on women's lives and the use of experimental avoidance.

Reference	Year	Sample	Method	Results / Conclusions
Greil, Shreffler, Schmidt & McQuillan (2011) USA	2011	n = 1027 of which primary infertility (399) and secondary infertility (628). No treatment,	Telephone interviews. Quantitative study.	Both types of infertility (primary and secondary) have been associated with high levels of psychological distress. Levels of depression and anxiety do not vary depending on the type of infertility or intentionality of women.
Hasanpoor-Azghdy, Simbar & Vedadhir (2014) Iran (Asia)	2014	n = 25 women with primary infertility and secondary infertility under treatment.	Semi-structured interviews. Qualitative study.	Iranian infertile women undergoing treatment face several psychological and emotional problems. Failure to treat infertility causes a decrease in self-esteem. The fear of not disappointing your husband involves higher levels of anxiety. After failed treatments or long time spent in treatment, it produces symptoms of depression, anxiety and negatively affects self-esteem.
Kahyaoglu & Balkanli (2015) Turkey (Asia)	2015	n = 89 infertile women under IFV treatment.	Questionnaires. Cross-sectional quantitative study.	Symptoms of depression and anxiety are present in infertile women. Moreover, during treatment and especially after a failed treatment, anxiety and depression levels increase.
Maroufizadeh, Karimi, Vesali & Samani (2015) Iran (Asia)	2015	n = 330 of which 208 infertile women undergoing failed ART treatment.	Questionnaires. Cross-sectional quantitative study.	Women who have failed treatments suffer from higher levels of anxiety and depression than women who have not received any treatment. Anxiety reaches its maximum level after a single treatment failure and depression after two failures.
Massarotti et al. (2019) Italy (Europe)	2019	n = 89 infertile women before and after IVF treatment.	Questionnaires for the effects of treatment. Quantitative study.	The time spent trying to get pregnant and the fear of undergoing an unknown treatment are the causes of anxiety before exposure to a tratment. During treatment, anxiety levels decreased.
Ogawa, Takamatsu & Horiguchi (2011) Japan (Asia)	2011	n = 83 infertile women before treatment.	Self-reporting and evaluation questionnaires. Quantitative study.	Infertile women without a job and women undergoing treatment experience higher levels of depressive symptoms. Age is negatively associated with depression. The duration of infertility is not associated with anxiety and depression.

Reference	Year	Sample	Method	Results / Conclusions
Ramezanzadeh et al. (2004) Iran (Asia)	2004	n = 370 infertile women under treatment.	Questionnaires. Cross-sectional quantitative study.	Depression is significantly related to the causes of infertility, duration of infertility, educational level and vocational level. Anxiety is related to the duration of infertility and educational level. Anxiety and depression are more common after 4-5 years
Shahraki, Ghajarzadeh & Ganjali (2019) Iran (Asia)	2019	n = 189 infertile women before IVF treatment.	Questionnaires. Cross-sectional quantitative study.	Women with primary or secondary infertility do not differ in their levels of depression and anxiety. Failed treatment and feeling of helplessness cause depression and anxiety.
Tan et al. (2008) Germany (Europe)	2008	n = 115 untreated PCOS infertile women.	Questionnaires. Quantitative study.	The intentionality of infertile women (whether they want to conceive or not) is related to depression. Selfesteem is affected by the ability to conceive. Levels of anxiety and depression are higher in the first year of trying to get pregnant.
Verma et al. (2015) India (Asia)	2015	n = 280 infertile women under treatment.	Questionnaires. Case-control quantitative study.	Employed infertile women with a higher level of education and support from their husbands and families appear to be better protected from depressive and anxiety symptoms. Treatment increases the level of depression and anxiety.

Infertile women suffer from higher levels of anxiety and depression but also from lower self-esteem compared to fertile women (Begum & Hasan, 2014; Facchin et al., 2019; Maroufizadeh et al., 2015). A study in Poland, using the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI), showed that 35.44% of infertile women suffer from depression and anxiety compared to 19.47% of fertile women (Drosdzol & Skrzypulec, 2009). Another study in Chile, measuring BAI and the Rosenberg Self-Esteem Scale (RSES), found that 55.8% of infertile women had low self-esteem, 42.5% had low levels of anxiety, 10% moderate anxiety and 47.5% severe anxiety (Contreras et al., 2016). In the case of Asian population, 46% of infertile women, according yo BDI, experienced depressive symptoms (Fazardi & Ghasemzadeh, 2008).

Another study in Asia (Iran) showed, using the Cattle questionnaires for anxiety and depression and BDI, that between 67 and 84% of infertile women suffer from anxiety and 24-36% of infertile women suffer from depression (Ramezanzadeh et al., 2004). The instrument used by these studies were the same, except for the study in Iran which used another questionnaire to measure anxiety.

Infertile women are more prone to both the development of depresive and anxiety symptoms and lower self-esteem, but the psychological impact that infertility has on women differs depending on age (Drosdzol & Skrzypulec, 2009; Ogawa et al., 2011; Ramezanzadeh et al., 2004), level of education (Drosdzol & Skrzypulec, 2009; Ramezanzadeh et al., 2004; Verma et al., 2015), employment (Drosdzol & Skrzypulec, 2009; Ogawa et al., 2011: Ramezanzadeh et al., 2004: Verma et al., 2015), duration of infertility (Donkor et al., 2017; Drosdzol & Skrzypulec, 2009; Hasanpoor-Azghdy et al., 2014; Maroufizadeh et al., 2015; Ramezanzadeh et al., 2004; Tan et al., 2008; Verma et al., 2015), the type of infertility (Greil et al., 2011; Shahraki et al., 2019), known or unknown cause of infertility (Drosdzol & Skrzypulec, 2009; Ramezanzadeh et al., 2004), intentionality (Greil et al., 2011; Tan et al., 2008), perceived support (Begum & Hasan, 2014; Fazardi & Ghasemzadeh, 2008; Greil et al., 2011; Hasanpoor-Azghdy et al., 2014; Ramezanzadeh et al., 2004; Verma et al., 2015), treatment for infertility (Begum & Hasan, 2014; Hasanpoor-Azghdy et al., 2014; Kahyaoglu & Balkanli, 2015; Maroufizadeh et al., 2015; Massarotti et al., 2019; Ogawa et al., 2011; Shahraki et al., 2019; Verma et al., 2015).

Age

Age seems to be a predictor of depressive and anxious symptoms among women suffering from infertility. Research on the population of Poland and the US has shown that the aging of infertile women causes increases in depression and anxiety because they feel they do not have much time to conceive a child and their "biological clock" ticks (Drosdzol & Skrzypulec, 2009; Greil et al., 2011). Other research in Japan suggest that aging may influence the development of depression, but the results have not been clear (Ogawa et al., 2011). On the other hand, studies in Iran have had different results, showing that the symptoms of depression and

anxiety were more severe in infertile women aged 21 to 25 years (Ramezanzadeh et al., 2004). Two other studies on women in Italy and Turkey, which investigated the relationship between the psychological impact of infertility and age, found no connection between them (Kahyaoglu & Balkanli, 2015; Massarotti et al., 2019).

Level of education

As with age, education may be a predictor of symptoms of depression and anxiety. A higher level of education seems to have a positive effect on the mental health of women with infertility. Education has a protective effect against depression, more precisely, the higher the level of education, the lower the symptoms of depression and anxiety, therefore, women with lower levels of education are more prone to the psychological consequences of infertility (Drosdzol & Skrzypulec, 2009; Ramezanzadeh et al., 2004; Verma et al., 2015). However, a study on infertile women in Turkey found no association between the level of education and the psychological effects of infertillity (Kahyaoglu & Balkanli, 2015).

Employment

Employee status and occupational role are likely to have a positive impact on the psychological well-being of infertile women. The workplace can bring role satisfaction or help women suffering from infertility forget about their problems and focus their attention on occupational tasks (Drosdzol & Skrzypulec, 2009). The association is discussed in various studies that have shown that employed women had much lower levels of depression and anxiety than women who did not have a job (Drosdzol & Skrzypulec, 2009; Ogawa et al., 2011; Ramezanzadeh et al., 2004; Verma et al., 2015). In addition, having a job reduces the stress and anxiety caused by IVF treatments for infertility (Ramezanzadeh et al., 2004). However, the study conducted on infertile women in Pakistan showed no association between work activity and symptoms of depression and anxiety (Begum & Hasan, 2014).

Duration of infertility

The duration of infertility has been associated, in most research, with depression and anxiety (Donkor et al., 2017; Drosdzol & Skrzypulec, 2009; Hasanpoor-Azghdy et al., 2014; Maroufizadeh et al., 2015; Ramezanzadeh et al., 2004). Regarding self-esteem, no data were found to confirm a possible association (Hasanpoor-Azghdy et al., 2014). Three studies from Iran and an article from Ghana support the above statement, namely that anxiety and depression increase with increased duration of infertility (Donkor et al., 2017; Hasanpoor-Azghdy et al., 2014; Maroufizadeh et al., 2015; Ramezanzadeh et al., 2004). There is the fear of aging without the posibility of becoming pregnant and, therefore, the fear of loding their husband, which contributes to the development of anxiety (Donkor et al., 2017).

The 3-6 year period is the most critical, according to a study in Poland, in which anxiety and depression reach their highest levels, and the period of less than a year or more than 6 years of infertility seems to be less destructive and with a very high impact for infertile women (Drosdzol & Skrzypulec, 2009). Another study found that, in fact, the first year of infertility is the most difficult and most emotionally and mentally impacted by coping mechanisms that could "dampen" the experience of infertility over time (Tan et al., 2008). However, there are also studies that have shown no correlation between the duration of infertility and the mental health of women with infertility (Massarotti et al., 2019; Ogawa et al., 2011).

The type of infertility

By type of infertility, we refer to primary and secondary infertility. In this case, there were two contradictory results regarding the association between the type of infertility and the psychological impact of infertility. On the other hand, no connection between the variables was identified in a study in Iran, therefore, no differences were found between women with primary infertility and those with secondary infertility in terms of depression and anxiety (Shahraki et al., 2019).

On the other hand, in the US research, women with primary infertility suffered from higher levels of anxiety and depression compared to women with secondary infertility (Greil et al., 2011). Emotional needs may differ between women with primary infertility and women with secondary infertility (Greil et al., 2011). It is possible that women who have not had more pregnancies are more affected by infertility than women who already had at least one child before the diagnosis of infertility, due to the fact that latter are already mothers and can satisfy, in to some extent, the desire for motherhood, while women with primary infertility have never experienced such a thing (Greil et al., 2011).

Known or unknown cause of infertility

There are discrepancies in the results of the literature on the impact of knowing the cause of infertility on infertile women. One study in Poland, showed that infertile women who know the causes of their infertility experience higher cases of depression compared to women who do not know the cause of infertility (Drosdzol & Skrzypulec, 2009). In the other direction, according to an article from Iran, depression is more common in women with unknown causes of infertility (Ramezanzadeh et al., 2004). Whereas, anxiety is more common in women with endometriosis than in other causes of infertility (Ramezanzadeh et al., 2004).

Intentionality

Intentionality represents the presence or absence of the current desire to conceive. The literature suggests that this factor would be a predictor of anxiety and depression among infertile women. (Greil et al., 2011; Tan et al., 2008). Infertile women who have a current desire for a pregnancy experience higher levels of both anxiety and depression compared to women who do not have this desire at the time of the infertillity episode, according to the US research (Greil et al., 2011). Other findings in Germany on infertile women diagnosed with Polycystic Ovary Syndrome (PCOS) have suggested that although infertile women who have a desire to conceive suffer from more psychological problems when it comes to anxiety and depression, intentionality is not associated so strong with these symptoms (Tan et al., 2008).

Perceived support

Perceived sleep was considered one of the most important risk factors among women suffering from infertility (Begum & Hasan, 2014; Fazardi & Ghasemzadeh, 2008; Hasanpoor-Azghdy et al., 2014; Ramezanzadeh et al., 2004). Most research has highlighted the positive effect of support from husband, family and friends, so lack of support and care from others would raise anxiety and depression and lower self-esteem on infertile women (Begum & Hasan, 2014; Contreras et al., 2016; Fazardi & Ghasemzadeh, 2008; Hasanpoor-Azghdy et al., 2014; Ramezanzadeh et al., 2004; Verma et al., 2015). Also, the negative reactions and attitudes of the spouse or relatives seem to worsen the situation (Fazardi & Ghasemzadeh, 2008; Ramezanzadeh et al., 2004). According to a study in Iran, social support not only helps to alleviate psychological problems but rather, infertile women who perceived a high level of social support showed no signs of depression or anxiety (Ramezanzadeh et al., 2004).

These results are not confirmed in the US study, which claims that not every kind of support is a positive support (Greil et al., 2011). Women who receive support from family and friends feel guilty for not being able to provide for a child, which helps develop anxiety problems but, to a lesser extent, depression (Greil et al., 2011). Encouragement to seek treatment may be perceived as "pressure" from others, and perceived social pressure may be more stressful than supportive (Greil et al., 2011). However, although the perceived pressure from the family may lead to greater suffering, there is also the possibility that more affected women may seek more encouragement from others (Greil et al., 2011).

Treatment for infertility

Undergoing infertility treatment is another important risk factor in terms of the psychological consequences of infertility on women (Hasanpoor-Azghdy et al., 2014; Massarotti et al., 2019). Women undergoing infertility treatment experience higher levels of anxiety and depression (Begum & Hasan, 2014; Hasanpoor-Azghdy et al., 2014; Kahyaoglu & Balkanli, 2015; Maroufizadeh et al., 2015; Ogawa et al., 2011; Verma et al., 2015). Feelings of helplessness increase as the time spent on treatment

increases, this contributes to the development of symptoms of depression and anxiety among women with infertility, and the increase of the number of treatment exposure is associated with impaired "mind-body" connection and of psychological health (Hasanpoor-Azghdy et al., 2014; Kahyaoglu & Balkanli, 2015; Verma et al., 2015). Infertility is very common in women from lower social classes who most likely do not have the ability to bear the costs of treatment, since these costs are covered only partially or perhaps not covered by health insurance, therefore the costs of treatment and social determinants play an important role in the development of the psychological consequences of infertility (Hasanpoor-Azghdy et al., 2014). Anxiety and depression are less common in IVF treatments compared to other types of treatments (Hasanpoor-Azghdy et al., 2014).

Contrary to the data presented so far, a study of infertile women in Italy showed that anxiety and depressive symptoms decrease during treatment (Massarotti et al., 2019). This decrease in psychological consequences is explained by feelings of empowerment due to exposure to a process that could help or solve infertility problems and this effect could help infertile women to be more open about the social support they receive from the others (Massarotti et al., 2019).

Following a failed treatment, the situation becomes even more critical, as self-esteem is predicted to decrease among infertile women duet o feelings of helplessness and because they attribute blame and responsability for the failure of treatment considering that this body does not cope and is not good enough to support a pregnancy (Hasanpoor-Azghdy et al., 2014). Anxiety reaches its maximum level after a failed treatment, and in the case of depression, the peak is reached after two failures of infertility treatments, therefore, the levels of depression and anxiety are much higher after treatments and during treatment (Hasanpoor-Azghdy et al., 2014; Maroufizadeh et al., 2015; Ogawa et al., 2011; Shahraki et al., 2019).

DISCUSSIONS

Family status is important and valuable for most individuals. Having a child stabilizes the family and increases marital satisfaction (Ramezanzadeh et al., 2004). The absence of a child in the family can

cause relationship problems, such as divorce or extramarital affairs (Drosdzol & Skrzypulec, 2009) but also psychological problems such as depression, anxiety and low self-esteem (Contreras et al., 2016; Tan et al., 2008).

Infertile women suffer from higher levels of anxiety and depression compared to women in the fertile group (Tan et al., 2008). Among infertile women, 38% suffer from depression, 57.5% from anxiety and 55.8% have low self-esteem.

The desire to be a parent and not be able to achieve this goal does not directly influence the development of depressive symptoms, instead, a childless lifestyle ca contribute to the emergenge of social, sexual and couple concerns and these may include difficult emotional states (Galhardo et al., 2019). Women learn to take responsability and blame for their infertillity problems. They try to solve the problem but feelings of guilt, self-blame, loneliness and/or fear of losing their husband contribute to the development of symptoms of depression and anxiety.

When they see that their friends have managed to become mothers and when they are talking about their children, these is a possibility that depression levels will increase because they remind them of their reproductive problems and that they may not manage to get pregnant (Donkor et al., 2017). At the same time, not having children could influence how they are seen by others and some women feel worried because they feel they are seen as inferior and do not meet society's standards for the concept of woman-mother, which increases the probability of occurrence of psychological consequences and decreased self-esteem (Donkor et al., 2017; Facchin et al., 2019; Massarotti et al., 2019).

In some situations, women prefer to hide infertillity issues and at the same time use experiential avoidance as a way to stay in touch with these aversive experiences, but in some cases, experiential avoidance can contribute to the formation of depressive symptoms (Galhardo et al., 2019). The likelihood of developing or worsening psychological problems associated with infertility is influenced by certain risk factors such as age, level of education, employment, duration of infertility, type of infertility, known or unknown cause of infertility, intentionality, perceived social support and treatment for infertility.

Most research has shown that aging, low levels of education, lack of employment, current desire to conceive and lack of social support contribute to increased levels of depression and anxiety. The level of education has a protective role against depression, educated women being less prone to depression.

Although most studies analyzing age and level of education have shown a relation between the affective problems and infertility, there were some contradictory results who stated that there was, in fact, no connection (Kahyaoglu & Balkanli, 2015; Massarotti et al., 2019). Nevertheless, they are aware of the fact that having a larger sample size could change the results (Kahyaoglu & Balkanli, 2015).

The relationship between employment and infertility is discussed in various studies, stating that an occupational role seems to have a positive impact on the emotional and psychological health of women suffering from infertility. Nonetheless, according to Begum & Hasan (2014), "working status appeared as an insignificant predictor of depression and anxiety" (p. 1290). However, in their study, there was not presented any data regarding employment, nor an explanation for the given conclusion.

As presented in the literature analyzed earlier, the perceived support from the husband, relatives or friends because the lack of support from them but also from society can lead to psychological problems and low self-esteem. However, the support received from others is not always a positive support, for example, encouragement can be seen as a "pressure", and this social pressure may not be beneficial for women with infertility. Understanding how social support works and the ability to identify what type of support can increase or decrease psychological stress is important for the counseling process and future directions of treatment.

Regarding the duration of infertility, most research has shown that depression and anxiety increase with increased duration of infertility, other studies have considered the 3-6 year period of infertility as the most critical, and before the first year of infertility and after 6 years of infertility these symptoms improve significantly. Contrary to these results, in the study on the German population, the first year of infertility was seen as the most difficult and with a greater emotional impact and after the first year, the coping mechanisms intervene and "dampen" the experience of infertility (Tan et al., 2008).

For the type and cause of infertility, there were conflicting results. On the one hand, no differences were found in the research in Iran between women with primary infertility and women with secondary infertility, altough, as in the case of age and level of education, they justify these results by the existence of a limited sample size. However, the US study claims that women with primary infertility suffer from more psychological consequences because their emotional needs may differ, and women with secondary infertility were more likely to experience motherhood compared to women who did not have a previous pregnancy (Greil et al., 2011). Regarding the causes of infertility, the study on Polish women claims that women know the cause of their infertility suffer more (Drosdzol & Skrzypulec, 2009), and the study on Iranian women showed that, in fact, depression is more common in women with unknown causes of infertility (Ramezanzadeh et al., 2004). However, it is important to note that Drosdzol & Skrzypulec (2009) refer to the cause of infertility as female/male/combined, while Ramezanzadeh et al. (2004) in addition to female/male/combined infertility, they also analyze causes such as endometriosis, PCOS and so on.

The most important risk factor, that the literature has noted, for emotional problems amongst infertile women, was treatment for infertility. Women undergoing infertility treatments suffered from much higher levels of anxiety and depression compared to women who did not follow these treatments. However, anxiety levels initially decrease in women undergoing treatment because they feel they are doing something to solve their reproductive problems (Massarotti et al., 2019). Treatment costs could be a source of stress for infertile women with lower socioeconomic status. Undergoing a great number of treatments, increased time spent in treatment and, especially, treatment failure creates feelings of hopelessness and helplessness which contributes to worsening depressive symptoms and low self-esteem (Hasanpoor-Azghdy et al., 2014). Anxiety reaches its maximum level after a failed treatment, and in the case of depression, the peak is reached after two failed treatments (Maroufizadeh et al., 2015).

It is necessary that during the treatments for infertility, the psychological effects that occur throughout their period to be investigated and ameliorated. Due to the fact that the post-treatment period is the most critical and significant for infertile women, both counseling for these women and providing adequate support to improve the experience and psychological consequences should be considered.

Infertility is a problem that causes a great emotional and psychological impact, not only on the infertile woman, but also on her husband, relatives and friends. Therefore, if partners learn to support each other, this experience will bring them closer and strenghten the marital relationship. It was confirmed that infertile women reported better mental health when the relationship with their husband was closer and more supportive (Drosdzol & Skrzypulec, 2009). Mental compatibility is also a factor that affects the quality of life on infertile women (Onat & Beji, 2012).

Limitations and future directions of research

In this paper only depression, anxiety and self-esteem were assessed, therefore, a complete view of all the psychological problems that infertile women suffer from was not provided. It would have meant going through a much more complex process if all the psychological effects of women with reproductive problems had been taken into account and researched. At the same time, the physical, social or financial consequences of infertility have not been included, and these consequences, although not psychological, could influence the psychological impact of infertility. Therefore, a systematic review of all psychological effects would be of great necessity, but also the consideration of including the other consequences for trying to understand the differences that occur in the mental health of infertile women.

It is necessary to include women from different socio-economic backgrounds, as there are differences in their experiences. Risk factors, treatment and the experience of women under different treatments should be analyzed longitudinally.

Only studies published in journals and in English were reviewed. By excluding unpublished studies and those in languages other than English, there is a risk of omitting some information that may be relevant and important to this research. In addition, some studies with potential eligibility could not be accessed because the full version of the text could not be found.

CONCLUSIONS

The results of this systematic review showed that infertility has a negative psychological impact on women, moreover, almost half of women with reproductive problems suffer from high levels of anxiety and depression but also from low self-esteem. Of course, these experiences differ from woman to woman, but most of the time, the lifestyle and physical and mental health of infertile women is negatively affected.

Nine risk factors were found in the literature as having an influential role in women's experience with infertility. These factors are age, level of education, employment, duration of infertility, type of infertility, known or unknown cause of infertility, intentionality, perceived social support and treatment for infertility. After an in depth analysis of the studies included in this review, it can be seen that the results, somehow, confirm the mediating effect of these factors for the relationship between infertility and depression, anxiety and self-esteem. There were some conflicting results that, in some cases, were explained by the sample size limitation but, in other cases, there was no explanation or data supporting those results.

Beliefs regarding the social, cultural and sexual aspects of infertility are addressed in the literature as having an important role in women's life. When examining the emotional and psychological consequences of infertility, these concerns appear to be crucial in the way women cope with the diagnosis of infertility.

The results showed that it is important to consider counseling for improving quality of life and treating the emotional health issues of both women who are undergoing treatment or who have had failed treatments, but also women who are not under treatment. At the same time, it is necessary to advise family members to provide a broader understanding of the situation and experience but also to improve the quality of relationships.

Of the 17 studies included in this review, most studies focused on the analysis of depression (n = 15), but also on the study on anxiety level (n = 14), and very few articles studies self-esteem in association with infertility (n = 4). Of these studies, 15 of them were quantitative and 2

qualitative. Future research should be done to study the impact of infertility on women's health, including all psychological consequences, for a more complete look at the experiences of infertile women. At the same time, consideration should be given to including all the consequences that women with reproductive problems suffer.

REFERENCES

- Ali, H. S., Shams, H., Kessani, L. V., & Ali, R. (2015). DEPRESSION. *The Professional Medical Journal*, 22(11), 1480-1484. http://scholar.googleusercontent.com/scholar?q=cache:SsJdwFHs7goJ:scholar.google.com/&hl=ro&as_sdt=0,5
- Allan, H. T. (2013). The anxiety of infertility: the role of the nurses in the fertility clinic. *Human Fertility*, *16*(1), 17-21. https://doi.org/10.3109/14647273. 2013.778423
- Asociația pentru Reproducere Umană din România. (2018, 18 June). Retrieved from https://www.arur.ro/2018/06/18/855/
- Begum, B. N., & Hasan, S. (2014). Psychological problems among women with infertility problem: a comparative study. *J Pak Med Assoc*, 64(11), 1287-91. https://www.ipma.org.pk/PdfDownload/7075
- Carreño-Meléndez, J., Henales-Almaraz, M. C., & Sánchez-Bravo, C. (2011). Self esteem and self concept in women with infertility. *Perinatología y Reproducción Humana*, *25*(1), 29-38. https://www.medigraphic.com/pdfs/inper/ip-2011/ip111f.pdf
- Contreras-García, Y., Jara-Riquelme, V., & Manríquez-Vidal, C. (2016). Description of anxiety, hopelessness and self-esteem levels in a group of Chilean women diagnosed with primary infertility: A pilot study. *Revista Colombiana de Obstetricia y Ginecología*, 67(1), 50-60. http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0034-74342016000100006
- Cousineau, T. M., & Domar, A. D. (2007). Psychological impact of infertility. *Best Practice & Research Clinical Obstetrics & Gynaecology*, *21*(2), 293-308. https://doi.org/10.1016/j.bpobgyn.2006.12.003
- Cunningham, N., & Cunningham, T. (2013). Women's experiences of infertility—towards a relational model of care. *Journal of clinical nursing*, *22*(23-24), 3428-3437. https://doi.org/10.1111/jocn.12338
- Díaz Bernal, Z., & García Jordá, D. (2011). Gender perspective and the physicianpatient relationship in treating infertility. *Revista Cubana de salud pública*, 37, 106-109. https://www.scielosp.org/article/rcsp/2011.v37 n1/106-109/es/

- Donkor, E. S., Naab, F., & Kussiwaah, D. Y. (2017). "I am anxious and desperate": psychological experiences of women with infertility in The Greater Accra Region, Ghana. *Fertility research and practice*, *3*(1), 6. https://link.springer.com/article/10.1186/s40738-017-0033-1
- Drosdzol, A., & Skrzypulec, V. (2009). Depression and anxiety among Polish infertile couples an evaluative prevalence study. *Journal of Psychosomatic Obstetrics & Gynecology*, *30*(1), 11-20. https://doi.org/10.1080/01674 820902830276
- Dural, O., Yasa, C., Keyif, B., Celiksoy, H., Demiral, I., Yuksel Ozgor, B., ... & Bastu, E. (2016). Effect of infertility on quality of life of women: a validation study of the Turkish FertiQoL. *Human Fertility*, *19*(3), 186-191. https://doi.org/10.1080/14647273.2016.1214754
- Facchin, F., Buggio, L., Dridi, D., & Vercellini, P. (2019). A woman's worth: the psychological impact of beliefs about motherhood, female identity, and infertility on childless women with endometriosis. *Journal of Health Psychology*, 1359105319863093. https://doi.org/10.1177/1359105319863093
- Farzadi, L., & Ghasemzadeh, A. (2008). Two main independent predictors of depression among infertile women: an Asian experience. *Taiwanese journal of obstetrics and gynecology*, 47(2), 163-167. https://www.sciencedirect.com/science/article/pii/S1028455908600741
- Galhardo, A., Alves, J., Moura-Ramos, M., & Cunha, M. (2019). Infertility-related stress and depressive symptoms—the role of experiential avoidance: a cross-sectional study. *Journal of reproductive and infant psychology*, 1-12. https://doi.org/10.1080/02646838.2019.1612046
- Global prevalence of infertility, infecundity and childlessness. (2014, November 28). Retrieved January 27, 2020. https://www.who.int/reproductivehealth/topics/infertility/burden/en/
- Greil, A. L., Shreffler, K. M., Schmidt, L., & McQuillan, J. (2011). Variation in distress among women with infertility: evidence from a population-based sample. *Human Reproduction*, *26*(8), 2101-2112. https://academic.oup.com/humrep/article/26/8/2101/646885
- Hasanpoor-Azghdy, S. B., Simbar, M., & Vedadhir, A. (2014). The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. *Iranian journal of reproductive medicine*, 12(2), 131. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 4009564/
- Kahyaoglu Sut, H., & Balkanli Kaplan, P. (2015). Quality of life in women with infertility via the Ferti QoL and the Hospital Anxiety and Depression Scales. *Nursing & health sciences*, *17*(1), 84-89. https://doi.org/10.1111/nhs.12167

- Maroufizadeh, S., Karimi, E., Vesali, S., & Samani, R. O. (2015). Anxiety and depression after failure of assisted reproductive treatment among patients experiencing infertility. *International Journal of Gynecology & Obstetrics*, 130(3), 253-256. https://doi.org/10.1016/j.ijgo.2015.03.044
- Massarotti, C., Gentile, G., Ferreccio, C., Scaruffi, P., Remorgida, V., & Anserini, P. (2019). Impact of infertility and infertility treatments on quality of life and levels of anxiety and depression in women undergoing in vitro fertilization. *Gynecological Endocrinology*, *35*(6), 485-489. https://doi.org/10.1080/09513590.2018.1540575
- Moore, H. L. (1991). *Anthropology and feminism* (Vol. 3). Universitat de València.
- Ogawa, M., Takamatsu, K., & Horiguchi, F. (2011). Evaluation of factors associated with the anxiety and depression of female infertility patients. *BioPsychoSocial medicine*, *5*(1), 15. https://link.springer.com/article/10.1186/1751-0759-5-15
- Onat, G., & Beji, N. K. (2012). Effects of infertility on gender differences in marital relationship and quality of life: a case-control study of Turkish couples. *European journal of obstetrics & gynecology and reproductive biology*, 165(2), 243-248. https://doi.org/10.1016/j.ejogrb.2012.07.033
- Ramezanzadeh, F., Aghssa, M. M., Abedinia, N., Zayeri, F., Khanafshar, N., Shariat, M., & Jafarabadi, M. (2004). A survey of relationship between anxiety, depression and duration of infertility. *BMC women's health*, *4*(1), 9. https://bmcwomenshealth.biomedcentral.com/articles/10.1186/1472-6874-4-9
- Sañudo Toca, L. (2014). Consequences of infertility/sterility in woman's health. [Master's thesis, Escuela Universitaria de Enfermería "Casa Salud Valdecilla"] https://repositorio.unican.es/xmlui/bitstream/handle/10902/5195/SañudoTocaL.pdf?sequence=1
- Shahraki, Z., Ghajarzadeh, M., & Ganjali, M. (2019). Depression, Anxiety, Quality of Life and Sexual Dysfunction in Zabol Women with Infertility. *Mædica*, 14(2), 131. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6709388/
- Tan, S., Hahn, S., Benson, S., Janssen, O. E., Dietz, T., Kimmig, R., ... & Elsenbruch, S. (2008). Psychological implications of infertility in women with polycystic ovary syndrome. *Human Reproduction*, *23*(9), 2064-2071. https://academic.oup.com/humrep/article/23/9/2064/2914513
- Verma, P., Rastogi, R., Sachdeva, S., Gandhi, R., Kapoor, R., & Sachdeva, S. (2015). Psychiatric morbidity in infertility patients in a tertiary care setup. *Journal of clinical and diagnostic research: JCDR*, 9(9), VC01. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4606317/

- Wilkins, K. M., Warnock, J. K., & Serrano, E. (2010). Depressive symptoms related to infertility and infertility treatments. *The Psychiatric Clinics of North America*, 33(2), 309-321. https://doi.org/10.1016/j.psc.2010.01.009
- Zegers-Hochschild, F., Adamson, G. D., de Mouzon, J., Ishihara, O., Mansour, R., Nygren, K., ... & Van der Poel, S. (2009). The international committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary on ART terminology, 2009. *Human reproduction*, 24(11), 2683-2687. https://doi.org/10.1093/humrep/dep343