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A SYSTEMATIC REVIEW ON DROPOUT OF INFERTILITY TREATMENTS AND RELATED FACTORS

Dea Nabila Ratu Alicia*

**Faculty of Medicine, University of Malahayati, Indonesia*

Corresponding Author:
deanabilaratu@gmail.com

Abstract

Infertility occurs when a couple has been unable to produce a child for a period of at least one year while engaging in regular sexual activity and not using any kind of birth control. In addition, the pair must not have used any form of contraception during that time period. Fecundity is defined as a woman's ability to carry a pregnancy to full term without experiencing complications. Studies conducted on populations indicate that the probability of a woman becoming pregnant at any given month ranges between 20 and 25 percent overall. It is difficult to compare dropout rates across different facilities and nations due to factors such as the expense of infertility treatments, the regulations that control payment, and the accessibility of these therapies. The overwhelming majority of fertility specialists are obsessed with the outcomes of therapy and the success rates of their patients, but they frequently ignore or forget about the "invisible" individuals who withdraw from treatment. There is a lack of clarity regarding the causes and factors that lead individuals to quit focusing on their relationships. Many married couples find that they are better off financially if they choose to forego having any more children. During the period of mourning that is linked with an inability to produce children, undergoing at least one cycle of in vitro fertilization (IVF) may be performed as a "ritual." Several studies have found a correlation between dropout and a number of factors, some of which are as follows: emotional factors, communication issues, delaying treatment, physical and psychological burden, personal problems, refusal to accept treatment, problems related to the infertility organization and clinics, marital issues, age of women, number of previous births, previous unsuccessful treatments, poor treatment prognosis, child adoption, spontaneous pregnancy, and lack of insurance coverage are among the factors that have been found.

Keyword: *Drop Out; Infertility; In Vitro Fertilization (IVF); Ovulation; Pregnancy*

INTRODUCTION

Infertility occurs when a couple has been unable to conceive a child for a period of at least one year while engaging in regular sexual activity without the use of any form of birth control. The capacity of a woman to carry a pregnancy to term is referred to as her fecundity. According to studies of populations, the likelihood of a woman becoming pregnant at any given month ranges between 20 and 25 percent.[1] There is a 50-50 chance that a couple who has been diagnosed with infertility will conceive by the second or third year of treatment, while the remaining couples are classified as having an extremely difficult time conceiving.[2]

Infertility is a somewhat frequent disorder that can have a variety of causes, including those related to the woman, the man, or both. There is no recognized cause of infertility. The problem of infertility can have a significant impact on married couples who encounter it, including physical, economic, and psychological concerns as well as impacts on the couple's ability to have children. Infertile couples are typically subjected to a lengthy process of diagnosis and therapy, which can be both a psychological and a physical strain on the couple's lives.[3–5]

It is difficult to compare dropout rates between different facilities and countries because to factors such as cost, rules governing reimbursement, and accessibility to infertility treatments. The vast majority of fertility specialists are preoccupied with treatment results and success rates, yet they often overlook or forget about the "invisible" patients who withdraw from treatment.[6] As a result of the fact that passive dropout contributes to a decrease in cumulative success rates, medical practitioners typically work to prevent or reduce the phenomenon. The participative aspect of a patient's decision to stop receiving treatment is disregarded by the classification of dropout as either passive or active. The decision to stop fertility treatment is seldom ever researched.[7]

It is not apparent what causes and factors lead people to stop focusing on their relationships. The decision to stop having children is beneficial to many couples. At least one round of in vitro fertilization (IVF) can serve as a "ritual" during the grieving process associated with an inability to have children.[8] This is an act that one must force upon themselves in order to prevent the regret of "not having tried everything to have a child." This method is not present in the existing body of work. There is scant research on the causes of dropouts, both positive and negative. It is surprising to find out that an infertility clinic does not use a standardized discontinuance tool.[9,10]

This study's objective is to research the reasons or variables that lead patients to cease undergoing therapy for infertility and report its findings and conclusions.

METHODS

The author ensured that the study was carried out appropriately by adhering to the requirements provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. These rules ensured that the research was carried out appropriately. This is done in order to guarantee that the findings of this investigation are accurate. This literature review attempts to understand the cause or factor that contributes to patients discontinuing their infertility treatments by assessing or analyzing previous research on the subject. The basic idea of this paper is to emphasize how important the issues that have been brought up are to consider.

The following qualifications were required of the researchers who took part in the study: 1) In order for the paper to be accepted for publication, it must be written in English and the primary focus of the study must be on the cause or factor that contributes to patients dropping out of infertility treatment. 2) This assessment takes into account publications that were produced after 2018 but prior to the time period that is the focus of this systematic analysis. Examples of research that is not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are substantially identical to previously published journal papers.

We used "drop out" and "infertility treatments" as keywords.The search for studies to be included in the systematic review was carried out from February, 18th 2023 using the PubMed and SagePub databases by inputting the words: *("drop"[All Fields] AND "out"[All Fields] AND ("infertiles"[All Fields] OR "infertilities"[All Fields] OR "infertility"[MeSH Terms] OR "infertility"[All Fields] OR "infertile"[All Fields] OR "infertility s"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields])) AND (clinicaltrial[Filter] OR randomizedc-ontrolledtrial [Filter])* used in searching the literature.

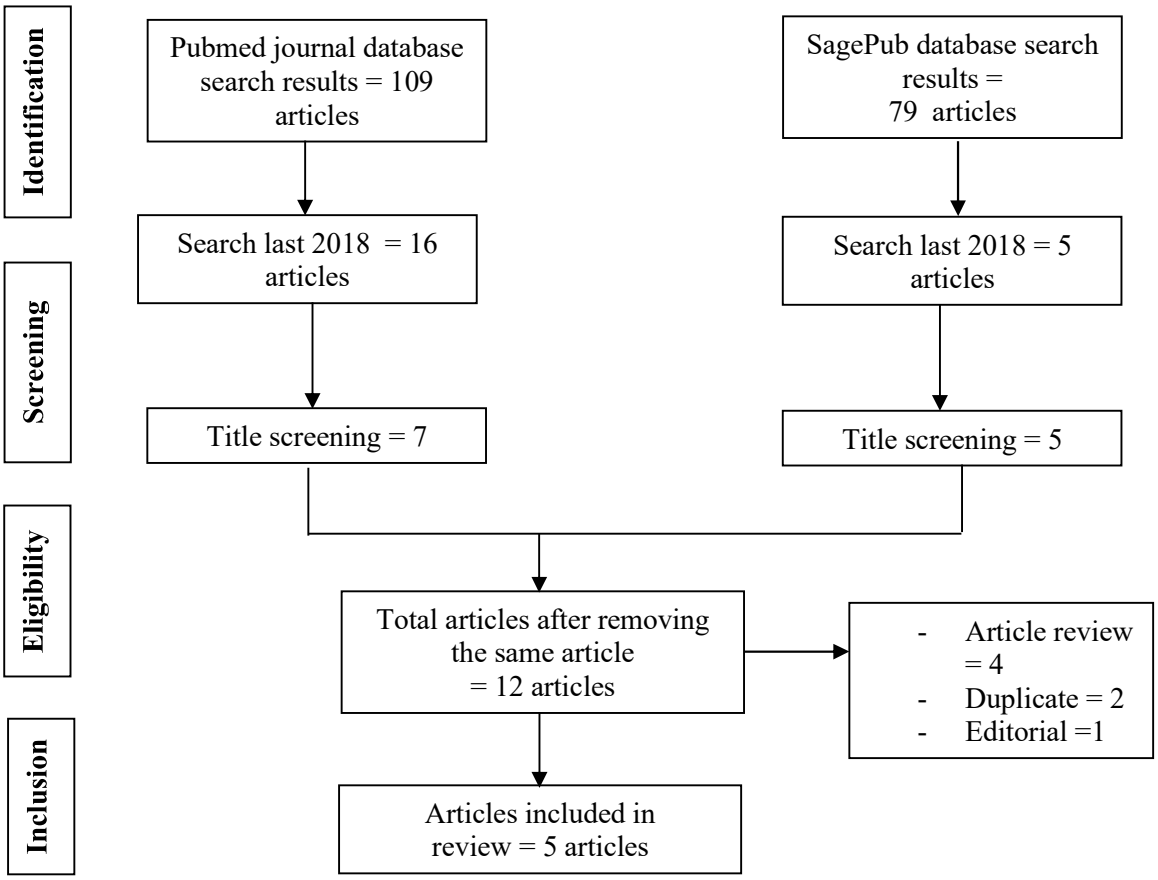

Figure 1. Article search flowchart

The authors assessed each study's eligibility based on its abstract and title. Then, the authors selected past studies for this paper. Reviewing many papers with the same pattern led to this result. English submissions must be unpublished. The systematic review included only studies that matched all criteria. The search only returns useful results. We ignore unsatisfactory research. The research will then be examined. This study found names, authors, publication date, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Before deciding which papers to look at in more depth, each author did their own study of the research listed in the title and abstract of the publication. Then, we'll look at all papers that meet the review's criteria for inclusion and are therefore good enough to be included. Then, based on what we found, we'll decide which papers to include in the review. Manuscripts are chosen to be evaluated based on this criterion. To make the process of choosing papers to review as easy as possible. Which previous studies were done, and what parts of those studies make them good enough to be included in the review?

RESULT

Domar, et al (2019)[9] showed reason patients dorp out from IVF. Of the 54 participants who had not sought continued therapy after one unsuccessful cycle, over half (52%) were taking a break from treatment, and nearly one-quarter (24%) could not afford the out-of-pocket payments. Losing insurance (22%), and conceiving spontaneously (22%). Participants who did not seek care after numerous unsuccessful cycles were more likely to be pursuing or have adopted a child (23% vs. 4%; P = 0.002), to report that continued treatment was too stressful (45% vs. 20%; P = 0.001), and to report being advised to cease therapy (15% vs. 4%; P = 0.03).

Dropout of infertility treatments is a regular phenomenon in IVF (In Vitro Fertilization) / ICSI (Intra cytoplasmic Sperm Injection) operations, and many patients want to avoid continuing infertility treatments. Ghorbani, et al (2020)[11] showed the choice of a couple to discontinue further treatment may have been influenced by a number of circumstances, including the emotional and physical strain, the strain on their finances, and the bad prognosis.

Other study by Ghorbani, et al (2021)[6] showed the incidence rate of infertility treatment abandonment was 42.9%. Number of unsuccessful treatments (P <0.001), age of women (p = 0.01), age of men (p = 0.02), and type of infertility (primary or secondary) (p= 0.004) were associated with cessation. Couples with a single unsuccessful treatment experience were more likely to abandon treatment (60.1%) than those with two or more unsuccessful treatments (21.7%).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Domar, 2019[9]	USA	Cross sectional study	237 insured patients who discontinued treatment after more than one unsuccessful cycle	Half of the participants who did not return to care within four months of a single unsuccessful IVF cycle stated that they were taking a vacation from treatment, and despite having partial or complete insurance coverage, nearly one-quarter stated that they did not return due to financial difficulties. Those who had endured a single unsuccessful treatment cycle experienced less treatment stress than those who had endured multiple unsuccessful cycles.
Ghorbani, 2020[11]	Iran	Retrospective cohort study	420 infertile women	The choice of a couple to discontinue further treatment may have been influenced by a number of circumstances, including the emotional and physical strain, the strain on their finances, and the bad prognosis.
Ghorbani, 2021[6]	Iran	Retrospective cohort study	380 infertile women	Infertility treatment dropout was common, and demographic factors affected treatment continuation. Couples with primary infertility and one failed treatment were more likely to drop out and its implications. Insufficient awareness and information may cause this.
Arhin, 2022[12]	Ghana	Cross sectional study	20 infertile women	The majority of the reasons cited by patients and healthcare professionals for discontinuing infertility treatment in a typical African setting are undocumented in existing studies. Patients and healthcare professionals shared both similar and diverse perspectives on the reasons for discontinuing infertility treatment.
Miller, 2021[13]	New Zealand	Retrospective cohort	974 couple	An actively managed IVF population can achieve a low dropout rate of 10%. This was lower than previously reported, indicating that prognosis, expense, and treatment management are major reasons for dropout in the general IVF population. Couples with several embryos may also require psychological assistance because to treatment weariness or multiple transfers.

Arhin, et al (2022)[12] showed the most common reasons for stopping infertility treatment were a lack of support from male partners, looking for alternative treatments, unfulfilled outcome expectations, unsatisfactory medical services, physical distance, social stigma, and moving away from the original treatment center. They asked patients and healthcare providers why infertile people stop fertility treatment before conceiving. It critically analyzes the data with reference to relevant literature to understand the answers, issues, and phenomena.

Miller, et al (2021)[13] showed there was a low IVF dropout rate between the first and second IVF cycles, with 10% of couples terminating treatment for stress-related reasons. By the completion of therapy, the cumulative live birth rate in this "low dropout" cohort was 59%, ranging from 72% (30 years) to 42% (38-39 years) depending on female age. The majority of patients who stopped due to stress had a positive prognosis, and one-third of them still had embryos in cryostorage. Just 30% of those who stopped using the paid counseling services did so.

DISCUSSION

This definition of infertility, also known as primary infertility, describes a situation in which a couple has been unable to produce a child for a period of at least one year while engaging in sexual activity outside of the context of any form of birth control. Secondary infertility is a term that refers to a person's inability to either conceive children or carry a pregnancy to term. Evaluation and treatment of women older than 35 years can be done after a marriage has been in place for at least six months.[14] Male and/or female variables can both play a role in causing infertility.[3]

About 35% of instances can be attributed to male variables and 35% can be attributed to female factors. Twenty percent of infertility can be attributed to a combination of male and female variables, but most of the time there is more than one component involved. The use of tobacco, marijuana, or other substances; excessive exercise; poor dieting associated with severe weight loss or gain; and old age are all lifestyle variables that have been linked to an increased risk of infertility. Other lifestyle factors that have been linked to an increased risk of infertility include environmental and occupational factors.[3,14]

The frequency of primary infertility was higher than that of secondary infertility, which was 42.5%. Primary infertility accounted for 57.5% of all cases. 46.6% of instances were attributed to female causes, with polycystic ovarian syndrome

(PCOS) being responsible for 46% of those cases. Infertility was seen in persons with PCOS who were either thin or overweight. There was a significant correlation between infectious factors, such as pelvic inflammatory illness and tuberculosis (P = 0.001), and tubal factor infertility.[15]

As people got married later in life, the factors that contributed to infertility changed. PCOS was the most common cause of infertility among couples who had been married for less than five years; however, male factor and unexplained infertility were the most common causes among couples who had been married for longer than five years. Tobacco and alcohol usage were significantly connected with abnormal semen reports, which accounted for 20% of all infertility cases. Male variables were responsible for 20% of all infertility cases (P = 0.001).[15]

Patients who were diagnosed as infertile during the first year have an 85 percent chance of conceiving during the second year. Ovulation, pregnancy, and live birth rates can be raised by up to 73% when clomiphene citrate is administered at a dose of 50 mg per day for five days at the beginning of the cycle, followed by an increased dose of up to 150 mg per day. There was no significant difference in pregnancy rates at 6 months after expectant management or IIU (with stimulation), according to the findings of a long-term, randomized study conducted in the Netherlands on patients with a moderate prognosis.[3,14]

The desire to become parents is a powerful motivator for couples who seek treatment at an infertility clinic. Parenting is an essential developmental milestone. Some patients do not complete their therapy despite the staff's best efforts, and the reasons for this are not completely understood. If experts can get an understanding of the phenomena of couples dropping out of fertility therapy, they will be able to assist couples in resolving challenges in decision making and give a more personalised and sympathetic approach to reproductive treatments.[16]

It can aid couples in the decision-making process they go through together to make decisions that are educated and healthy for their particular circumstance. In order to gain a better understanding of the phenomena known as "dropout" in infertility therapy. These reasons were derived from the existing body of research and included the following: the occurrence of a spontaneous pregnancy; the burden of relational or social relationships; the lack of an acceptable choice of treatment; the psychological and physical burdens; the support and expertise of the staff at the fertility center; the financial cost; the woman's age; medical considerations; and an alternative realization of the woman's wish to have a child (e.g. adoption).[16]

Age is a factor that might be viewed as being more sensible in the choice to discontinue therapy for females. In point of fact, there was a favorable correlation between the female age and the female age as a cause to stop therapy. It is highly likely that these women either had personal objections to continuing treatment at their age or that they were counseled by the gynecologist to consider discontinuing therapy. This is due to the fact that the majority of treatment centers in Belgium rarely offer treatment to females who are older than 43.[16]

As compared to the physical burden, the psychological burden was a more significant factor in the decision to discontinue therapy. It would appear that the emotional toll that comes along with reproductive therapy has a significant bearing on the choice that women make to discontinue treatment.[17] Many patients feel a significant amount of psychological load not only while undergoing fertility therapy, but also after receiving a diagnosis of infertility and during the course of the clinical study of infertility.[18]

Many research have sought to determine why individuals cease fertility therapy, with psychological load being listed as one of the most prevalent causes.[16,19] However, in the current study, non-cooperation of male partners was one of the key reasons that caused patients to quit therapy, as reported by patients and healthcare providers. Due to the fact that men and women contribute nearly equally to the causes of infertility,[20] such views on the part of males provide a challenge when assessing and evaluating infertile couples. In spite of these findings, in many areas of the world, both men and women are hesitant to blame infertility to the male partner, a feature considered to contribute to the low number of males seeking fertility therapy.[12,21]

Surprisingly, financial problems were not given as a reason to stop treatment. When we did our study in Belgium, most of the cost of the medicine to stimulate the ovaries was covered, but the lab costs for IVF/ICSI were not covered and patients had to pay a lot per cycle (about 1,500–2,000 EUR). Couples who think that money will be a problem may never think of fertility treatment as a real option for them. Cost could be a reason why someone doesn't start treatment, but it shouldn't be a big reason why someone stops treatment. Also, for many couples, the goal of getting pregnant and having a baby may be more important than any extra costs.[16]

Studying treatment discontinuation in government-funded IVF can give insight into the psychological and physiological aspects that, in addition to cost, incline patients to drop out of their IVF cycles. This is because the stress of financial responsibility is a primary contributor to cycle dropout. It has been demonstrated that between 12 and 40 percent of couples stop therapy after a first financed IVF cycle, despite the fact that they are eligible for future sponsored treatment. These findings come from studies of care that has been funded by either the government or insurance companies.[13,22,23]

Considering the outcome of the first unsuccessful IVF cycle, the proportion of early abandonment was relatively high (54%) when the initial IVF effort failed (0 or 1 oocyte retrieved and no embryo transfer). When the first stage was successful, there were no discernible variations in early abandonment based on the subsequent steps of a failed IVF treatment (fresh embryo transfer, frozen embryo transfers, pregnancy). The increased dropout rate among women with no or few recovered oocytes is consistent with two prior trials conducted in Britain and France.[23]

Remarkably, the risk of discontinuation rose as the number of frozen embryos grew, despite the fact that a big number of frozen embryos is a positive prognostic indicator. Couples may not undergo a fresh IVF treatment in France if they have embryos from a prior round stored. The increased rate of discontinuation among couples with a large number of frozen embryos may be attributable to a greater degree of burden in these couples as a result of several transfers; however, this only applies to a relatively small number of couples in our study.[23]

The factors that were associated with a higher risk of early discontinuation were also those that are well known to be associated with impaired chances of successful IVF treatment. These factors include an older age of the woman, a longer duration of infertility, and a low ovarian response to hormonal stimulation that led to the retrieval of 0 or 1 oocyte during the first failed attempt at IVF treatment.[23]

Approximately one quarter of couples who had stopped treatment after the first unsuccessful IVF and who participated in the postal follow-up research indicated a view of a poor prognosis or the psychological load of therapy. This was the most common reason given by these couples for their decision to stop treatment. It is therefore plausible that patients' self-diagnosed poor prognoses contribute to a rise in their levels of stress, and that the combination of these two variables, patients' self-diagnosed poor prognosis and increased stress, leads to a higher risk of early IVF discontinuation.[6,9]

Yet, self-identified negative prognosis is an entirely distinct idea from 'medically diagnosed poor prognosis'. According to the findings of a number of studies, a sizeable portion of the couples who gave a negative prognosis as the reason for the dissolution of their relationship actually had a positive prognosis. When objective medical variables connected with early IVF cessation are studied, patients with poor prognostic qualities have a greater likelihood of terminating therapy after a first unsuccessful IVF attempt (independent of the rationale for discontinuation). This is true even if the IVF attempt was unsuccessful.[6,9]

CONCLUSION

Couples may discontinue therapy for a variety of reasons, such as emotional and physical distress, financial constraints, or a dismal prognosis. It appears that educational and supportive programs on psychological, economic, therapeutic, demographic, and personal issues could be useful in reducing the number of individuals who abandon their infertility treatment before its completion.

REFERENCE

[1]. ASRM. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2013;99(1):63.
[2]. Fainberg J, Kashanian JA. Recent advances in understanding and managing male infertility. F1000Research. 2019;8.
[3]. Cunningham FG; et al, Cunningham FG; Leveno KJ; Bloom SL; et al, F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe BLH. Williams Obstetri. 25th ed. New York: The McGraw-Hill Companies; 2020.
[4]. Simionescu G, Doroftei B, Maftei R, et al. The complex relationship between infertility and psychological distress (Review). Exp Ther Med. 2021;306(3):198–202.
[5]. Datta AK, Campbell S, Felix N, Nargund G. Accumulation of embryos over 3 natural modified IVF (ICSI) cycles followed by transfer to improve the outcome of poor responders. Facts, views Vis ObGyn. 2019 Mar;11(1):77–84.
[6]. Ghorbani M, Hoseini FS, Yunesian M, Keramat A. Dropout of Infertility Treatments Among Iranian Infertile Couples: A Cohort Study. 2021;
[7]. Ghorbani M, Hoseini FS, Salehin S, Talebi SS, Keramat A. A supportive randomized clinical trial on Iranian infertile women with the history of infertility treatments dropout following unsuccessful ART cycle/s: A study protocol. Heliyon. 2023;9(3).
[8]. Dueholm Hjorth IM, Kristensen SG, Dueholm M, Humaidan P. Reproductive outcomes after in vitro fertilization treatment in a cohort of Danish women transplanted with cryopreserved ovarian tissue. Fertil Steril. 2020 Aug;114(2):379–87.
[9]. Domar AD, Rooney KL, Dodge LE. Determining the reasons why insured women drop out of IVF treatment after one unsuccessful cycle. Fertil Steril. 2019;112(3):e398.
[10]. Vaiarelli A, Cimadomo D, Gennarelli G, Guido M, Alviggi C, Conforti A, et al. Second stimulation in the same ovarian cycle: an option to fully-personalize the treatment in poor prognosis patients undergoing PGT-A. J Assist Reprod Genet. 2022;39(3):663–73.
[11]. Ghorbani M, Hosseini FS, Yunesian M, Keramat A. Dropout of infertility treatments and related factors among infertile couples. Reprod Health [Internet]. 2020;17(1):192. Available from: https://doi.org/10.1186/s12978-020-01048-w
[12]. Arhin SM, Mensah KB, Agbeno EK, Azize DA, Henneh IT, Agyemang E, et al. Pharmacotherapy of infertility in Ghana: Why do infertile patients discontinue their fertility treatment? PLoS One [Internet]. 2022 Oct

17;17(10):e0274635. Available from: https://doi.org/10.1371/journal.pone.0274635
[13]. Miller LM, Wallace G, Birdsall MA, Hammond ER, Peek JC. Dropout rate and cumulative birth outcomes in couples undergoing in vitro fertilization within a funded and actively managed system of care in New Zealand. Fertil Steril [Internet]. 2021;116(1):114–22. Available from: https://www.sciencedirect.com/ science/article/pii/ S001502822 1000625
[14]. ASRM. Endometriosis and infertility: a committee opinion. Fertil Steril. 2012;98:591–8.
[15]. Kella AA; Despande SB. Pulmonary surfactants and their role in pathophysiologi of Lung Disorders. Indian J. 2013;5–22.
[16]. Van den Broeck U, Holvoet L, Enzlin P, Bakelants E, Demyttenaere K, D'Hooghe T. Reasons for Dropout in Infertility Treatment. Gynecol Obstet Invest [Internet]. 2009;68(1):58–64. Available from: https://www.karger.com/ DOI/10.1159/000214839
[17]. Domar AD. Impact of psychological factors on dropout rates in insured infertility patients. Fertil Steril. 2004;81 (2) :271–3.
[18]. Eugster A, Vingerhoets AJJM. Psychological aspects of in vitro fertilization: a review. Soc Sci Med.1999;48(5): 575–89.
[19]. Domar AD, Smith K, Conboy L, Iannone M, Alper M. A prospective investigation into the reasons why insured United States patients drop out of in vitro fertilization treatment. Fertil Steril. 2010;94(4):1457–9.
[20]. Deshpande PS, Gupta AS. Causes and prevalence of factors causing infertility in a public health facility. J Hum Reprod Sci. 2019;12(4):287.
[21]. Dhont N, Luchters S, Ombelet W, Vyankandondera J, Gasarabwe A, Van de Wijgert J, et al. Gender differences and factors associated with treatment-seeking behaviour for infertility in Rwanda. Hum Reprod. 2010;25(8):2024–30.
[22]. Gameiro S, Verhaak CM, Kremer JAM, Boivin J. Why we should talk about compliance with assisted reproductive technologies (ART): a systematic review and meta-analysis of ART compliance rates. Hum Reprod Update. 2013;19(2):124–35.
[23]. Troude P, Guibert J, Bouyer J, de La Rochebrochard E, Group D. Medical factors associated with early IVF discontinuation. Reprod Biomed Online. 2014;28(3):321–9.