

# Impacts and Causes of Female Infertility: An Observational Study

## Aditi Mishra<sup>1</sup>, Manish Dev Sharma<sup>1\*</sup>, Archna Tandon<sup>2</sup>, Farah Ahsan<sup>3</sup>, Rajesh Rayal<sup>4</sup>, Naveen Gaurav<sup>1</sup> and Pankaj Negi<sup>5</sup>

<sup>1</sup>Department of Biotechnology, School of Basic and Applied Sciences, Shri Guru Ram Rai University, Patel Nagar, Dehradun- 248001, Uttarakhand, India. <sup>2</sup>Department of Gynaecology and Obstetrics (IVF Specialist), Shri Mahant Indiresh Hospital, Dehradun-248001, Uttarakhand, India. <sup>3</sup>Department of Biochemistry, Shri Mahant Indiresh Hospital, Dehradun-248001, Uttarakhand, India. <sup>4</sup>Department of Zoology, School of Basic and Applied Sciences, Shri Guru Ram Rai University, Patel Nagar, Dehradun-248001, Uttarakhand, India. <sup>5</sup>Department of Pharmacy, DIT University, Dehradun-248009, Uttarakhand, India. \*Corresponding author: sharma.manishdev@gmail.com

## ABSTRACT

Male and female infertility is one of the medical, physiological, and emotional factors among couples willing to have a child. It is defined unable to achieve pregnancy after regular intercourse for 12 months without using any protection (contraceptive pills or condoms). There are many factors that work as a barrier to the couple for a successful conception. These factors could be environmental, lifestyle, past medical history, and emotional. About 15 to 20% of a couple of their reproductive age are currently suffering from this trauma in India only. Not having a child, consider an isolated or cut-off person in society which ultimately affects not only the mental status of the couple as well as sociological effects. This is an observational study in which we counter many demographic and reproductive factors, those work as an obstacle to a successful pregnancy in couples. That couple who are of their reproductive age, visiting an IVF center has a bundle of emotions and stress with them along with new hope to be pregnant. Infertility has been also related to some other factors like physical conditions, environmental conditions, psychological issues, and also acquired risk factors. In females, Menstrual disorders, past medical history, hormonal disorders, overweight/obesity, and many demographic factors, and habits, play a significant role in causing infertility. The average length of the marriage of infertile couples, their duration of infertility, and sterility at the first visit to the infertility clinic has been also considered. The couples who had experienced at least one of the assisted reproductive techniques such as microinjection, intrauterine infusion (IUI), and in-vitro fertilization (IVF) are included in this study. During this study period, All the infertile women who had diagnostic laparoscopy for primary infertility were included and the female who had less than 12 months of marriage or who had pregnancy at least once were excluded. Different environmental, physiological, and psychological conditions emphasized the need to study the different causes of female and male infertility in each area.

Keywords: Female infertility, Past medical history, Hormonal disorder, BMI, AST

## **INTRODUCTION**

Globally, every year 60-80 million couples suffer from infertility, out of which about 15-20 million are in India alone (Sudha and Reddy, 2013). The term infertility means "inability to give birth or produce", which is a worldwide issue that affects people around the world. The causes of infertility may differ according to the medical conditions, Environmental conditions, geographical/demographic location and socio-economic condition, lifestyle, etc. (Deyhoul et al., 2017). It is a multiplex disorder with a combination of physical, psychological, medical, psychosocial, and economic problems (Olooto et al., 2012). It can also define as, a failure in gaining pregnancy in couples after 12 months of unprotected sexual intercourse (Deyhoul et al., 2017). Some other authors state it as, the inability of a couple to achieve pregnancy over an average period of one year (in a woman under 35 years of age) or 6 months (in a woman above 35 years of age) despite adequate, regular (3-4 times per week), unprotected sexual relationship with one man is called infertility (Olooto et al., 2012). In any society where having a child, defines a woman's identity and motherhood plays a significant role, infertility can create damage to the women, socially and emotionally (Sudha and Reddy, 2013). Infertility can be due to the woman and man, or both, it could be primary or secondary. If the couple has never been conceived called primary infertility, whereas, in secondary infertility, there is difficulty in conceiving after having conceived (either bared the pregnancy or had a termination or miscarriage) (Olooto et al., 2012). Infertility is a medical condition that can cause mental, psychological, physical, and spiritual destruction to infertile couples. This condition, Infertility, emotionally affects both partners whether the patient could be male or female (Walker and Tobler, 2021). The causes of infertility by medical conditions are ovulation defects, uterus-related issues, tube blockage, hormonal imbalance, endometriosis, menstrual disorders, and past medical conditions. Many cases of infertility are related to ovulation defects as ovulation is necessary for the reproductive process and the luteinizing hormone or human chorionic gonadotropin is the key player in the induction of the whole process (Richards, 2007). Uterus-related concerns include impaired implantation which could be due to uterine anomalies, intra-uterine adhesions, or reduced endometrial receptivity (Kuohung and Hornstein 2011). Fallopian tubes are considered to be a fertilization spot for an ovum and sperm, any infection caused by chlamydia trachomatis, gonorrhea, or due to genital tuberculosis can cause damage to the fallopian tube and ultimately cause infertility (Torre et al., 2010; Briceag et al., 2015). Endometriosis is an estrogen-dependent

disorder (Finas et al., 2006), which is characterized by the presence of endometrial tissues inside or outside of the uterine cavity (Eskenazi and Warner, 1997). PCOD/PCOS is one of the most common types of menstrual disorder which can cause female infertility on the other hand there are many endocrine disorders like hypothyroidism, hyperthyroidism, hypoprolectemia, hyperprolactinemia and many more that could lead to female infertility (Cramer and Missmer, 2002). It has also been observed that infertility can be due to advanced age, overweight, or obesity. BMI, years of marriage, living together as well as most common types of medical conditions in infertile female has been included. This study aimed to determine the frequent causes of infertility in infertile couples.

#### MATERIALS AND METHODS

This observational study includes the 130 couples who visited the IVF center (Obstetrics and Gynaecology Department) in Shri Mahant Indiresh Hospital Patel Nagar Dehradun (Uttarakhand) from 2020 to 2022. Patients who have primary infertility and undergo at least one artificial reproductive technique (ART), like IUI, IVF, and ICSI are included in this study, and the couple who spends less than 12 months of togetherness, male-infertility related factors, underage females, and patients of secondary infertility are excluded from the study. An informed consent form is filled by the discussion with the couple and is to be signed after that. Complete hormonal profiling (LH, FSH, Oestrogen, progesterone, prolactin, creatinine, and TSH), including past medical history to be done after abdominal ultrasounds and laparoscopy. Some general investigations like taking height, weight, BP, and calculated BMI have been also performed (Aziz, 2010; Masoumi et al., 2015). These study findings are based on a verbal discussion and consent from a couple who visited IVF centers SMIH from 2020 to 2022 in Dehradun (Uttarakhand). All the tests have been performed by the VITROS XT 7600 in the Department of Biochemistry, Shri Mahant Indiresh Hospital, Patel Nagar Dehradun.

#### RESULTS

All 130 female patients in their premenopausal age (18-45) are included in this study. The patients who met our inclusion criteria are eligible for the purpose of our present findings (Al-Asadi and Hussein, 2015). Table 1 presented all the study participants, with their period of infertility, and the number and percentage of the participants who had to go through at least one of the assisted reproductive technologies (ART), like IUI or IVF. According to their years of infertility a total of 32 (25%) of the patients at 1-2 years of infertility, 56 (43%) of the patients at 5-9 years of infertility (highest), 7 (5%) of the patients at 10-14 years of infertility respectively (Figure 1). A total of 115 patients were seeking IUI treatment and 27 patients went for IVF (including only IVF/ after 3 failed attempts of IUI), while 8 patients stuck to the medications and pursued treatment and did not walk out. Table 2 shows the number and percentage of the patients who go through any medical condition likewise: a total of 14 patients out of which 4 (29%) patients at their 1-2 years of infertility after marriage, 1 (7%) at 3-4 years of infertility, 7 (50%) at 5-9 years of infertility, 1(7%) at 10-14 years and 1(7%) at more than 15 years of infertility due to Ovulation defects (Less egg formation/no egg formation), total 12 patients out of which 4 (33%) at 1-2 years of infertility, 1 (8%) at 3-4 years of infertility, 5 (42%) at 5-9 years of infertility,0 (0%) at 10-14 years of infertility and 2 (17%) at more than 15 years of infertility, due to uterus related problems (small size uterus/cholelithiasis uterus/Fibroid uterus) (Figure 2). A total of 22 patients had been gone through fallopian tube blockage problem, either one or both, out of which 3 (14%) at 1-2 years of infertility, 5 (23%) at 3-4 years of infertility, 12 (55%) at 5-9 years of infertility, 2 (9%) at 10-14 years of infertility and 0(0%) at more than 15 years of infertility after marriage. A total of 34 patients had been gone through hormonal imbalance (Thyroid/ FSH/LH/Prolactin/AMH), out of which 8 (24%) at 1-2 years of infertility, 10 (29%) at 3-4 years of infertility, 12 (35%) at 5-9 years of infertility, 0 (0%) at 10-14 years of infertility and 4 (12%) at more than 15 years of infertility after marriage. Total of 7 patients out of which 3 (43%) patients at their 1-2 years of infertility after marriage, 1 (14%) at 3-4 years of infertility, 0 (0%) at 5-9 years of infertility, 2(29%) at 10-14 years and 1(14%) at more than 15 years of infertility due to Endometriosis (tissues lines grow outside the uterus). 36 patients out of which 7 (19%) patients at their 1-2 years of infertility, 9 (25%) at 3-4

years of infertility, 19 (53%) at 5-9 years of infertility, 1 (3%) at 10-14 years and 0 (0%) at more than 15 years of infertility due to PCOS/PCOS (irregular periods). Total of 25 patients out of which 5 (20%) patients at their 1-2 years of infertility, 4 (16%) at 3-4 years of infertility, 13 (52%) at 5-9 years of infertility, 1 (4%) at 10-14 years and 2 (8%) at more than 15 years of infertility could be because of Rubella (viral positive) patients. Table 3 shows the total number and percentage of patients with common lifestyle factors - a total of 6 patients had advanced age (>35years), out of which 4 (67%) at 5-9 years of infertility and 2 (33%) at >15 years of infertility were observed. A total of 9 patients had husband-related problems (medical conditions/ low sperm count), out of which 1 (11%) at 1-2 years of infertility, 1 (11%) at 3-4 years of infertility, 4 (44%) at 5-9 years of infertility, 2 (22%) at 10-14 years of infertility and 1 (11%) at >15 years of infertility had been seen. A total of 3 patients were less sexually active, out of which 1 (33%) at 1-2 years of infertility, and 2 (67%) at 5-9 years of infertility were observed. A total of 9 patients had unexplained infertility, as 5 (56%) at 1-2 years of infertility, 1 (11%) at 3-4 years of infertility, 1 (11%) at 5-9 years of infertility, 2 (22%) at 10-14 years of infertility, and 2 (22%) at >15 years of infertility had been noted. Table 4 consists of demographic characteristics of infertile women on basis of their age like- in infertile females, those aged less than 30 years their average height was  $154 \pm 5.82$ , weight was  $60.89 \pm 10.37$ , and BMI was  $25.42 \pm 3.89$  respectively (Figure 3), while those were more than 30 years, their height was  $153 \pm 7.90$ , weight was 60.64  $\pm$ 9.32 and BMI were 25.96  $\pm$  4.13. while in fertile patients, less than 30 years old had an average height 152  $\pm$ 1.98, weight was 53.13  $\pm$ 3.92 and BMI was 22.86  $\pm$ 1.71, and those were more than 30 years old had height  $152 \pm 2.08$ , weight  $56.95 \pm 3.98$  and BMI was 24.55 $\pm 1.75$  respectively.

Table 1: Percentage	distribution	of the Fema	ale infertility	sample in a	clinical population
- insie if i er eentage					enneur population

Period of infertility (in Years) from (2020- 2021)	Total Patients (female) in a clinical population		No. of female patients undergo IUI		No. of fem undergo I	ale patients VF	No. of female patients pursuing treatment	
	Number	Percentage	Number	Percentage	Number	Percentage	number	%
1-2	32	25%	27	23%	9	33%	2	25%
3-4	27	21%	26	23%	3	11%	4	50%
5-9	56	43%	50	43%	8	30%	1	13%
10-14	7	5%	5	4%	4	15%	0	0%
>15	8	6%	7	6%	3	11%	1	13%
Total	130		115		27		8	

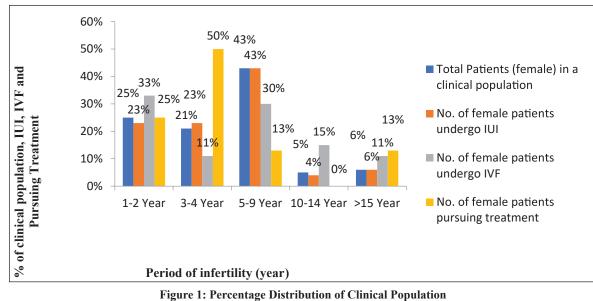


Table 2: Distribution of the Patients/sample according to a period of Infertility and nature of disorders
---

Period of			Types of Disorders (Medical Condition)											
Infertility (in years) Ovulation Defects		Rela	terus Tubal elated blockage roblems			Hormonal Endometriosis Deficiency		PCOD/ PCOS		Rubella				
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
1-2	4	29	4	33	3	14	8	24	3	43	7	19	5	20
3-4	1	7	1	8	5	23	10	29	1	14	9	25	4	16
5-9	7	50	5	42	12	55	12	35	0	0	19	53	13	52
10-14	1	7	0	0	2	9	0	0	2	29	1	3	1	4
>15	1	7	2	17	0	0	4	12	1	14	0	0	2	8
Total	14		12		22		34		7		36		25	

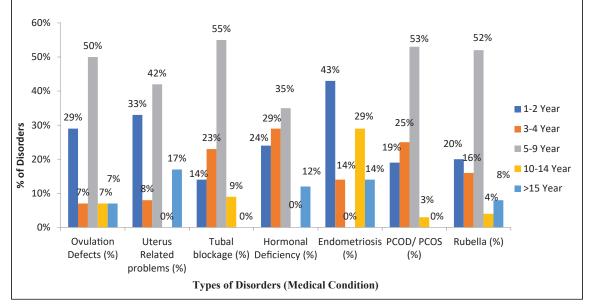


Figure 2: Types and Percentage of Disorders in infertility Patents.

Period of infertility (in years)	Advanced Age		Husband related problems		Sexually inactive		Unexplained infertility		
	No	%	No	%	No	%	No	%	
1-2	0	0	1	11	1	33	5	56	
3-4	0	0	1	11	0	0	1	11	
5-9	4	67	4	44	2	67	1	11	
10-14	0	0	2	22	0	0	2	22	
>15	2	33	1	11	0	0	0	0	
Total	6		9		3		9		

Table 3: Distribution of the Patients on the basis of some common factors

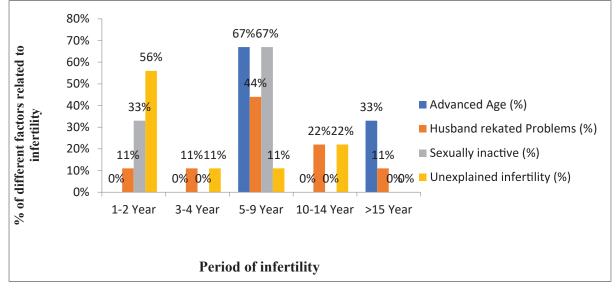


Figure 3: Distribution of some common factors related to infertility

 Table 4: Demographic characteristics of infertile women in each age group

Categories	Age	Height	Weight	BMI
Infertile	<30 Year	$154 \pm 5.82$	$60.89{\pm}10.37$	$25.42 \pm 3.89$
Female	>30 Year	$153 \pm 7.90$	$60.64 \pm 9.32$	25.96±4.13
Fertile	<30 Year	152±1.98	53.13±3.92	22.86±1.71
Female	<30 Year	152±2.08	$56.95 \pm 3.98$	24.55±1.75

## DISCUSSION

To get pregnant in advance ages are likely to be infertile. Many factors like Ovarian, tubal, uterus-related hormonal disorders, advanced age (over 35 years), medical conditions, and high BMI are the main factors that are involved in infertility in women, and changes in lifestyle can improve fertility which is also approved by many studies (Direkand-Moghadam et al., 2013). The stress which ended in depression in infertile women was high and they need more emotional support from their partners. It is further suggested that if infertile women can have a psychological assessment as a part of their medical treatment, then it could be a great step toward their mental health (Al-Asadi and Hussein, 2015). It is supported by many studies that a woman who has a longer time period of infertility shows a significantly much higher rate of depression compared with those who have less time period of infertility (Al-Asadi and Hussein, 2015; Kazandi et al., 2011; Ashkani et al., 2006). As my study suggests that the causes of infertility in older women may vary from younger women, such as those has a long time of their marriage and are over 35 years of age have more unexplained infertility, it is also supported by some other studies (Maheshwari et al., 2008; Chia et al., 2000). Some studies support that if a couple maintains a healthy lifestyle, normal body weight, normal BMI, and gets regular check-ups can avoid infertility-like issues (Sudha and Reddy, 2013).

## CONCLUSION

This study states that those patients who have 5-9 years of marriage are the maximum number of those suffering from infertility problem and goes for IUI, as compared with those who choose IVF. Family, medical and socioeconomic support is much needed for a woman who is trying to have a child over a long period of time. The major causes of female infertility are blocked fallopian tubes, PCOD/disorders of menstruation, hormonal imbalance, ovulation defects and could be rubella. Advanced age and unexplained infertility could be the reason for being infertile too. Higher BMI can also be a cause of infertility in couples. Family, medical and socio-economic support is much needed for a woman who is trying to have a child over a long period of time. Maintaining a healthy body, habits, and lifestyle can change the picture of infertility.

## ACKNOWLEDGEMENTS

The Authors are thankful to the Department of Biotechnology, School of Basic and Applied Sciences, Shri Guru Ram Rai University, and Department of Obstetrics and Gynaecology, Shri Mahant Indiresh Hospital, Patel Nagar, Dehradun Uttarakhand for supporting the study.

**Declaration:** We also declare that all ethical guidelines have been followed during this work and there is no conflict of interest among authors.

## REFERENCES

- Al-Asadi, J.N. and Hussein, Z.B. (2015). Depression among infertile women in Basrah, Iraq: Prevalence and risk factors. *Journal of the Chinese medical association*. 78(11): 673-677.
- Ashkani, H., Akbari, A. and Heydari, S.T. (2006). Epidemiology of depression among infertile and fertile couples in Shiraz, Southern Iran. *Indian Journal of Medical Sciences*. 60(10): 399-406.
- Aziz, N. (2010). Laparoscopic evaluation of female factors in infertility. J Coll Physicians Surg Pak. 20(10): 649-52.
- Briceag, I., Costache, A., Purcarea, V.L., Cergan, R., Dumitru, M., Sajin, M. and Ispas, A.T. (2015). Fallopian tubes–literature review of anatomy and etiology in female infertility. *Journal of medicine and life*. 8(2): 129.
- Chia, S.E., Lim, S.T.A., Tay, S. K. and Lim, S.T. (2000). Factors associated with male infertility: a casecontrol study of 218 infertile and 240 fertile men. BJOG: An International Journal of Obstetrics & Gynaecology. 107(1): 55-61.
- Cramer, D.W. and Missmer, S.A. (2002). The epidemiology of endometriosis. *Annals of the new york Academy* of Sciences. **955(1)**: 11-22.
- Deyhoul, N., Mohamaddoost, T. and Hosseini, M. (2017). Infertility-related risk factors: a systematic review. *Int J Women's Health Reprod Sci.* 5(1): 24-29.

- Direkvand-Moghadam, A., Delpisheh, A. and Khosravi, A. (2013). Epidemiology of female infertility; a review of literature. *Biosci. Biotechnol Res Asia.* 10(2): 559-67.
- Eskenazi, B. and Warner, M. L. (1997). Epidemiology of endometriosis. *Obstetrics and gynecology clinics of North America*. 24(2): 235-258.
- Finas, D., Hornung, D., Diedrich, K. and Schultze-Mosgau, A. (2006). Cetrorelix in the treatment of female infertility and endometriosis. *Expert Opinion on Pharmacotherapy*. 7(15): 2155-2168.
- Kazandi, M., Gunday, O., Mermer, T.K., Erturk, N. and Ozkınay, E. (2011). The status of depression and anxiety in infertile Turkish couples. *Iranian journal* of reproductive medicine. 9(2): 99.
- Kuohung, W. and Hornstein, M.D. (2011). Causes of female infertility. WHO Technical Report Series/W. Kuohung//Recent Advances in Medically Assisted Conception Number UpToDate. 16: 1-111.
- Maheshwari, A., Hamilton, M. and Bhattacharya, S. (2008). Effect of female age on the diagnostic categories of infertility. *Human Reproduction.* 23(3): 538-542.
- Masoumi, S.Z., Parsa, P., Darvish, N., Mokhtari, S., Yavangi, M. and Roshanaei, G. (2015). An epidemiologic survey on the causes of infertility in patients referred to infertility center in Fatemieh Hospital in Hamadan. *Iranian journal of reproductive medicine*. 13(8): 513.
- Olooto, W.E., Amballi, A.A. and Banjo, T.A. (2012). A review of Female Infertility; important etiological factors and management. J. Microbiol Biotech Res. 2(3), 379-385.
- Richards, J.A.S. (2007). Genetics of ovulation. In Seminars in reproductive medicine 25(4): 235-242. Copyright© 2007 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
- Sudha, G. and Reddy, K.S.N. (2013). Causes of female infertility: a cross-sectional study. *International Journal of Latest Research in Science and Technology*. 2(6): 119-123.
- Torre, A., Pouly J.L. and Wainer, B. (2010). Anatomic evaluation of the female of the infertile couple. *Journal de Gynecologie Obstetrique et Biologie de la Reproduction.* **39**: S34–S44.
- Walker, M.H. and Tobler, K.J. (2021). Female Infertility. *Stat Pearls [Internet]*. Treasure Island (FL): Stat Pearls Publishing; 2022 Jan-. Available from: https://www. ncbi.nlm.nih.gov/books/NBK556033/