

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20242498>

Original Research Article

An observational study on causes of female infertility

Ravi Chander Thatipelli^{1*}, Yashaswini Parunandi¹, Syed Nousheen¹, Suvarchala Shenkeshi¹,
Hijazi Fathima¹, Adaboina Anitha²

¹Department of Pharmacy Practice, Vaagdevi Pharmacy College, Bollikunta, Warangal, Telangana, India

²Department of Obstetrics and Gynaecology, Laxmi Narasimha Hospital, Hanamkonda, Warangal, Telangana, India

Received: 15 July 2024

Revised: 16 August 2024

Accepted: 17 August 2024

*Correspondence:

Ravi Chander Thatipelli,

E-mail: trc2884@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Infertility is characterized by the inability to conceive after 12 months or more of consistent, unprotected sexual activity. It can be caused by a variety of abnormalities of the female reproductive system. The aim is to study the causes of female infertility. The main objective is to identify the common causes and risk factors causing infertility in females.

Methods: The study population consisted of 383 infertile women. The study was conducted at Laxmi Narasimha hospital, Hanamkonda, in Warangal region for a period of 6 months. The tool used for the study was specifically designed questionnaire, which included the demographic data, and questions concerning the causes of infertility.

Results: Through our study it is observed that polycystic ovarian disease (PCOD), hypothyroidism, ovarian cyst, tubal damage, uterine abnormality, uterine fibroids, endometriosis are the causes of female infertility. The highest prevalence of infertility was found in patients with PCOD (30.5%), followed by patients with PCOD with other conditions (24%) (mostly PCOD with hypothyroidism). Highest prevalence of infertility in females was observed in the age group between 21-30 years. It is noticed that some patients were with infertility for unknown cause (16%).

Conclusions: In our study, we concluded that the PCOD is the major cause in both primary and secondary infertility in females. Higher prevalence of infertility was seen in age group of 21-30 years. Certain patients were having unexplained infertility. Infertility is now a widespread problem, and understanding the causes is the first step toward resolving it.

Keywords: PCOD, Hypothyroidism, Ovarian cyst

INTRODUCTION

Infertility is the disease of the reproductive system, characterized by the inability to conceive after 12 months or more of consistent, unprotected sexual activity. According to estimates, one out of every six people of reproductive age worldwide will experience infertility at some point in their lives. Infertility in the female reproductive system can be caused by a variety of abnormalities, including those of the uterus, ovaries, fallopian tubes, and endocrine system.

Infertility can be primary or secondary. Primary infertility is when a pregnancy has never been achieved by a person,

and secondary infertility is when at least one prior pregnancy has been achieved. A variety of factors can contribute to infertility. However, explaining the causes of infertility is not always possible. Infertility is caused by several factors like PCOD, thyroid disorders, ovarian cysts, uterine fibroids, uterine abnormalities, endometriosis, tubal damage.¹

Polycystic ovarian disease (PCOD) is distinguished by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology. PCOD affects fertility through infrequent ovulation or anovulation; reducing quality of oocytes; hyperandrogenism due to insulin resistance and hyperinsulinemia in PCOS patients lowers the levels of

hepatic sex hormone binding globulin; and due to functional deficiency of the endogenous action of FSH, the follicular growth is frustrated at different phases of maturation.²

Thyroid dysfunction can have a variety of effects on fertility, including: anovulatory cycles, luteal phase defect, excess prolactin (PRL). In case of hypothyroidism, the hypothalamus secretes more thyrotropin releasing hormone (TRH) when thyroid hormone levels are low. Increased TSH in hypothyroidism enhances pituitary secretion of PRL and thyroid stimulating hormone (TSH). GnRH neurons directly inhibit the release of GnRH when their PRL levels are elevated. The hypothalamic GnRH neurons that are inhibited result in anovulation, or decreased levels of LH and FSH. Ovulatory dysfunction and inadequate progesterone secretion from the corpus luteum during the luteal phase of the cycle are the consequences of this.³

Fatty or solid sacs or fluid filled pouch that develop inside or on the outside of one or both ovaries are called ovarian cyst. In order for fertilization and pregnancy to occur, the cyst may prevent the ovary from releasing an egg; Moreover, hormonal abnormalities brought on by cysts may influence ovulation; Moreover, pain and discomfort from ovarian cysts may make sexual activity challenging or impossible.⁴

Muscle tissue lumps in the uterus that are benign (non-cancerous) are called uterine fibroids. Uterine fibroids can affect fertility through changes in the shape of the cervix can alter the number of sperm that can enter the uterus; Modifications to the uterine shape may impede the sperm or embryo's ability to migrate; There may be an impact on blood flow to the uterine cavity. This may hinder an embryo's capacity to grow or adhere (implant) to the uterine wall.⁵

Congenital malformations of the female genital tract are deviations from normal anatomy resulting from embryological abnormal development of the Mullerian ducts. The endometrial mucosa covering the uterine septum responds poorly to estrogen, which results in poor proliferation and estrogenic maturation. This is because the uterine septum is thought to be composed of fibroelastic tissue with inadequate vascularization and an altered relationship between the myometrial and endometrial vasculatures. As a result, infertility or the loss of an early pregnancy may arise.⁶

Endometrial glands and stroma, which are functional tissue lining the uterus, can ectopically implant outside of the uterine cavity, a condition known as endometriosis, which is chronic and estrogen-dependent. It affects fertility by adhesions, chronic intraperitoneal inflammation, disturbed folliculogenesis, luteinized unruptured follicle, progesterone resistance, dysfunctional uterotubal motility.⁷

Normal fallopian tube function is a prerequisite for natural conception, as it is an essential component of union of the sperm. Tubal damage affects fertility by inflammation of the fallopian tubes, scarring of tissue and blockage of tube that prevents the egg from passing through the fallopian tube to reach the uterus.⁸

Through the process of atresia, the quantity of oocytes in the ovaries gradually and naturally diminishes. The female foetus has 6-7 million oocytes at 20 weeks of gestation, which is its maximal complement. Around 1-2 million oocytes are present at birth; this drops to 300,000-500,000 throughout puberty; 25,000 at age 37; and 1,000 at age 51, which is the average age of menopause.⁹

For obese women, hyperandrogenemia is a result of insulin resistance and hyperinsulinemia. Levels of leptin rise while those of growth hormone (GH), sex hormone-binding globulin (SHBG), and insulin-like growth factor binding proteins (IGFBP) drop. The hypothalamic-pituitary-gonadal (HPG) axis' neuro-regulation deteriorates as a result. Such changes could account for decreased ovulatory production and therefore for reproductive health issues.¹⁰

Stress prevents or lessens the anticipated rise in estrogen and luteinizing hormone (LH) surge, which delays follicular maturation and ovulation.¹¹

Infertility in men and women has been linked in several instances to parental consanguinity. It causes an early reduction in a woman's ovarian reserve, or her store of viable eggs. It results in chromosome Y abnormalities in males, which cause genetic defects in sperm. It has been demonstrated that women of consanguineous parents exhibit a very low ovarian reserve by the age of 20, which is typically present in women over the age of 40.¹²

METHODS

It is a retro-prospective observational study conducted at a Laxmi Narasimha hospital, Hanamkonda, Warangal district. This study was conducted for a period of 6 months, from July 2023 to December 2023, involving 383 subjects. Our study population included females of age 18-55 years, females with primary and secondary infertility, females with PCOD, thyroid disorders, ovarian cyst, uterine fibroids, endometriosis, uterine abnormalities, and hormonal imbalance. And excluded females who have undergone tubectomy, patients who are not willing to participate.

The data was collected through a questionnaire which included patient demographics details, fertility history, pregnancy history, sexual history, menstrual history, past medical history, laboratory investigations, family history, and social history.^{13,14} The data was collected with informed consent from patients. All the data was collected by conducting patient interviews and laboratory

investigations were studied and analysed. Data was entered in Microsoft excel and analysed using ANOVA.

RESULTS

In our study, we categorized the 383 patients into various age groups. The distribution of women across these age groups is as follows: 8.16% are in the 15-20 years age group, 40.46% are in the 21-25 years age group, 39.16% are in the 26-30 years age group, 10.7% are in the 31-35 years age group, and 1.5% are in the 36-40 years age group. The detailed age-wise distribution is illustrated in Figure 1.

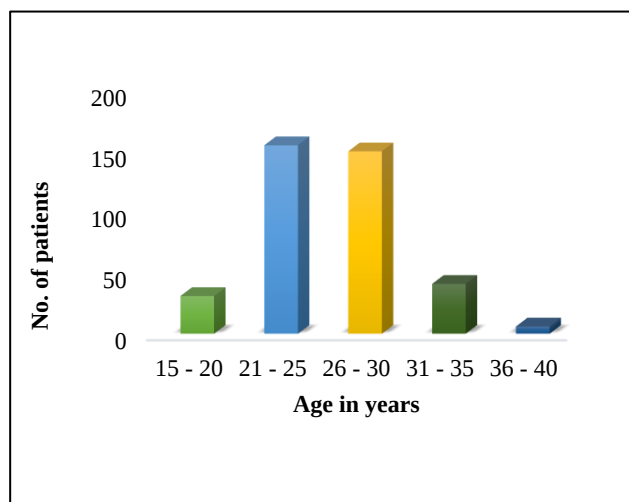


Figure 1: Distribution according to age.

Among the study population, 248 (65%) patients were of primary infertility and 135 (35%) patients were of Secondary infertility. In patients with primary infertility, prevalence was highest (Figure 2).

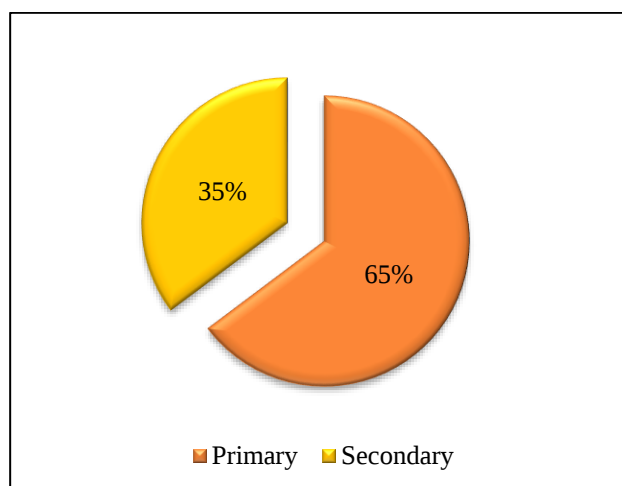


Figure 2: Distribution according to types of infertility.

Table 1 represents findings of distribution according to body mass index (BMI). Of these subjects, 50 (13%) patients had BMI range of 13-18.5 (Underweight), 203

(52%) patients had BMI range of 18.5-24.9 (Normal weight), 81 (21%) patients had BMI range of 25.0-29.9 (over weight) and 49 (13%) patients had BMI range of 30.0-36.0 (obese).

Among 383 patients, 135 patients had secondary infertility. Among them, 81 (60%) patients have had miscarriages and 48 (35%) patients have had C-section and 7 (5%) patients have had NVD as outcome of pregnancy delivery. Many patients with infertility have had history of miscarriages.

Among the 383 patients, 343 (90%) patients had knowledge regarding ovulation period and 40 (10%) patients have not had knowledge regarding ovulation period.

Of these 383 patients, 76 (20%) patients were consanguineous and 307 (80%) patients were non consanguineous.

As depicted in Figure 3, among the study population, 242 (63%) patients have had stress and 141 (37%) patients have no stress. The highest predominance of infertility was found in patients who had stress.

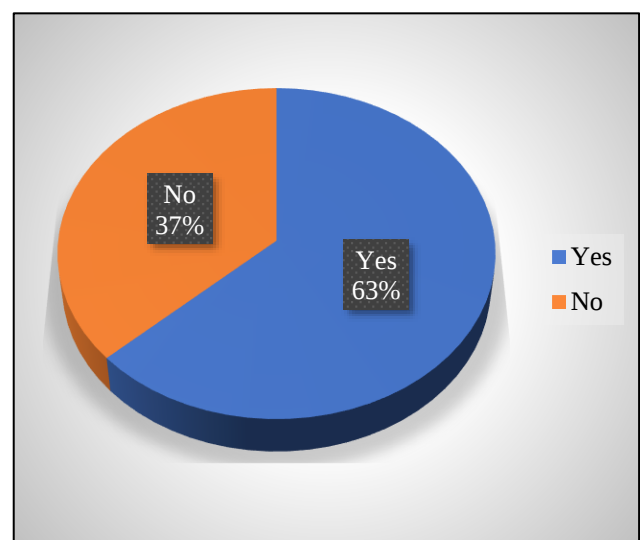


Figure 3: Distribution according to stress.

Figure 4 represents the information about causes of infertility. Among the study population, 117 (30.5%) of patients had PCOD, followed by 92 (24%) patients had PCOD with other conditions, 62 (16%) patients had unknown cause, 25 (6.5%) patients had ovarian cyst, 23 (6%) of patients were had hypothyroidism with other conditions, 23 (6%) patients had hypothyroidism, 14 (4%) patients had uterine fibroids, 13 (3.4%) patients had tubal damage, 9 (2.4%) patients had endometriosis, 4 (1.2%) patients had uterine abnormality. The highest prevalence of infertility was found in patients with PCOD, followed by patients with PCOD associated with other conditions. Lowest prevalence of infertility was found in patients with uterine abnormality.

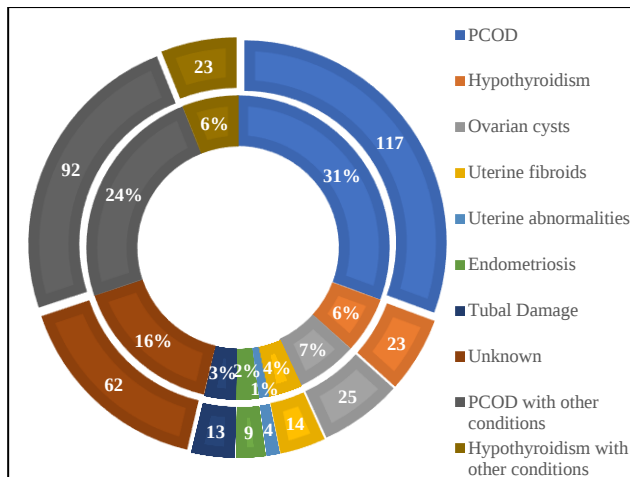


Figure 4: Distribution according to causes.

Table 4 revealed PCOD associated with other conditions causing infertility which included hypothyroidism, uterine abnormalities, uterine fibroids, tubal damage, ovarian cysts, endometriosis, diabetes, and hypertension. Of the PCOD associated with other conditions, PCOD with hypothyroidism (37 patients) was found to be the most prevalent cause of infertility.

Table 5 shows hypothyroidism associated with other conditions. In total participants included in the study, 23 patients had infertility due to hypothyroidism associated with other conditions. Among them, hypothyroidism associated with ovarian cysts and uterine abnormality (5 patients) was found to be the most prevalent cause of infertility.

Table 6 shows the age wise distribution of causes. Out of 383 patients, 117 patients had PCOD. Of these 117 patients, the highest prevalence of PCOD was found in 59 patients in 21-25 years age group, followed by 34 patients in 26-30 years age group. Least prevalence of PCOD was found in 1 patient with 36-40 years age group of patients.

Figure 5 depicts the causes according to types of infertility. In our study, PCOD was the most prevalent cause in patients with primary infertility (78) and the secondary

infertility (39). Uterine abnormalities (2) were the least prevalent cause in patients with primary infertility and endometriosis (1) was the least prevalent cause in patients with secondary infertility.

In the study population, 62 patients were identified with an unknown cause. Among these patients, 18% patients were consanguineous, and 82% patients non consanguineous.

In the 62 patients with unidentified cause, 51.6% patients in age group of 26-30 years had infertility. Infertility with unknown cause was then followed by 35.5% patients in age group of 21-25 years, 9.7% patients in age group of 15-20 years and none in age group between 36-40 years.

Among the 62 patients with unknown cause of infertility, 40 patients (65%) had normal weight, 12 patients (19%) had BMI of overweight, 7 patients (11%) had underweight, and 3 patients (5%) had obesity.

Among 62 patients with unknown cause, 36 patients (58%) were having stress and 26 patients (42%) were having no stress.

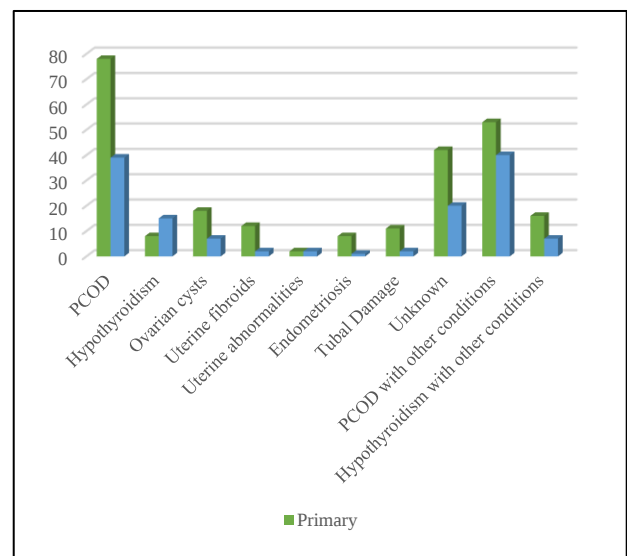


Figure 5: Distribution of causes according to types of infertility.

Table 1: Distribution according to BMI.

Category	No. of patients	Percentage (%)
Underweight	50	13
Normal	203	53
Overweight	81	21
Obese	49	13

Table 2: PCOD associated with other conditions.

PCOD associated with other conditions	No. of patients
PCOD, hypothyroidism	37
PCOD, uterine abnormalities	8
PCOD, uterine fibroids	5

Continued.

PCOD associated with other conditions	No. of patients
PCOD, tubal damage	6
PCOD, ovarian cysts	7
PCOD, endometriosis	1
PCOD, diabetes	1
PCOD, tubal damage, hypertension	2
PCOD, hypothyroidism, endometriosis	1
PCOD, ovarian cysts, endometriosis	5
PCOD, hypothyroidism, ovarian cysts	1
PCOD, hypothyroidism, uterine fibroids	6
PCOD, hypothyroidism, endometriosis, tubal damage	1
PCOD, uterine abnormalities, tubal damage	1
PCOD, uterine fibroids, ovarian cysts, tubal damage	1
PCOD, hypothyroidism, tubal damage, uterine fibroids, ovarian cysts	1
PCOD, hypothyroidism, uterine abnormalities	4
PCOD, ovarian cysts, uterine abnormalities, tubal damage	1
PCOD, tubal damage, uterine fibroids	1
PCOD, hypothyroidism, tubal damage	2

Table 3: Hypothyroidism associated with other conditions.

Hypothyroidism associated with other conditions	No. of patients
Hypothyroidism, uterine fibroids	3
Hypothyroidism, tubal damage	2
Hypothyroidism, tubal damage, uterine fibroids	1
Hypothyroidism, ovarian cysts	1
Hypothyroidism, ovarian cysts, uterine abnormality, uterine fibroids, tubal damage	2
Hypothyroidism, ovarian cysts, uterine abnormality	5
Hypothyroidism, ovarian cysts, tubal damage	1
Hypothyroidism, uterine fibroids, ovarian cysts	2
Hypothyroidism, uterine abnormality, uterine fibroids	3
Hypothyroidism, uterine abnormality, tubal damage	3

Table 4: Age wise distribution of causes.

Causes/age (in years)	15-20	21-25	26-30	31-35	36-40
PCOD	14	59	34	9	1
Hypothyroidism	-	13	7	3	-
Ovarian cysts	1	12	10	2	-
Uterine fibroids	-	-	2	9	3
Uterine abnormalities	-	1	3	-	-
Endometriosis	-	-	8	1	-
Tubal damage	-	3	8	2	-
Unknown	6	22	32	2	-
PCOD with other conditions	10	40	33	8	2
Hypothyroidism with other conditions	-	5	13	5	-

DISCUSSION

In our study involving 383 female patients with infertility, we gathered data through questionnaires and laboratory reports, covering various aspects including demographic details, fertility history, pregnancy history, sexual history, menstrual history, past medical history, and family history.

Our findings indicate that conditions such as PCOD, hypothyroidism, ovarian cysts, tubal damage, uterine abnormalities, uterine fibroids, and endometriosis are

significant contributors to female infertility. Among these, PCOD emerged as the most prevalent cause of the infertility.

Age also plays a critical role in infertility, with a notable decline in oocyte quantity in the ovaries as women age. Consistent with this, our study found that infertility rates were highest in women aged 21-25 years (40.46%) and 26-30 years (39.16%). This contrasts with findings by Mamatha et al who reported the highest infertility rate in the 26-30 years age group (38%).¹⁵

Additionally, our study found that primary infertility was more common, affecting 65% of patients, compared to 35% with secondary infertility. This is in contrast to Alawan et al study, which reported secondary infertility as more prevalent at 51.6%, while primary infertility was seen in 48.4% of cases.¹⁶

Regarding body mass index (BMI), our study observed a higher prevalence of infertility among patients with a normal BMI (52%). This is in contrast to Shinde et al findings, which indicated that 39% of infertile women had a normal BMI, while 61% had a high BMI.¹⁷

In our study, the highest prevalence of infertility was found in patients with PCOD in correspondence with studies conducted by Baby et al and Deshpande et al. PCOD is the major cause of female infertility 24.5% and 46% respectively.^{18,19}

In our study, 30.5% patients had PCOD, which is known to cause hyperandrogenism, reduced quality of oocytes, and anovulation; and subsequently leading to infertility.

And 24% participants had PCOD associated with other conditions. Of these populations, 37 patients had PCOD associated with hypothyroidism, the mechanism of how PCOD leads to hypothyroidism is unclear. In PCOD, increase in pro-inflammatory markers and increase in insulin resistance leads to decreased deiodinase-2 activity at pituitary level resulting in relative T3 deficiency and increase in TSH level, causing hypothyroidism. Thus, PCOD and Hypothyroidism together affecting the fertility.

The 6.5% patients had ovarian cysts. The cyst may prevent the ovary from releasing an egg and also causes hormonal imbalances which affects ovulation.

The 6% of participants had hypothyroidism. Hypothyroidism leads to elevated PRL levels, decreased levels of LH and FSH, which causes ovulatory dysfunction and inadequate progesterone secretion from the corpus luteum.

The 6% of participants had hypothyroidism associated with other conditions. Hormonal overlap in the pituitary feedback mechanism, as TSH, GH, FSH, and LH are all glycoprotein with common alpha chain and may thus cross-react. High-serum TSH mimics FSH and LH, leading to a luteinized ovarian cyst.

The 4% patients had uterine fibroids. Fibroids may cause modifications to the uterine shape which may impede the sperm or embryo's ability to migrate, obstruct the fallopian tube, and impact blood flow to the uterine cavity.

The 3.4% of patients had tubal damage, which is known to cause inflammation of the fallopian tubes, scarring of tissue and blockage of tube that prevents the egg from passing through the fallopian tube to reach the uterus.

The 2.4% patients had endometriosis, which causes adhesions, chronic inflammation, disturbed folliculogenesis, and dysfunctional utero-tubal motility.

The 1.2% of participants had uterine abnormalities, which may have an impact on endometrial receptivity, which may lead to implantation failure and early pregnancy loss or infertility.

In our study, 16% patients had infertility with unknown cause. Unexplained infertility is typically diagnosed in couples who have undergone all standard infertility investigations, such as ovulation tests, tubal patency, and sperm analysis. Unexplained infertility is diagnosed when tubal patency (hysterosalpingogram and/or laparoscopy) and normal ovulatory function (basal body temperature, cervical mucus changes, serum LH surge or mid-luteal progesterone) are confirmed.

Limitations

The study was restricted to a short duration. The study was conducted at a single study area. So, the results were limited to the study area and further studies should be performed at different study sites to conclude the causes of female infertility.

CONCLUSION

In our study, PCOD is the major cause of infertility in both primary and secondary infertility in females. Higher prevalence of infertility is seen in age group of 21-30 years. Prevalence of infertility was equal in obese as well as lean patients. There is a category called unexplained infertility which is also known as idiopathic which includes the population whose cause for infertility is not known. Infertility is now a widespread problem, and understanding the causes is the first step toward resolving it.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Radhi I, Al-Saadi NH, Wahid HHA. Female Infertility: A Systematic review of the Literature. *Indian J Publ Heal Res Develop.* 2019;10(5):457-61.
2. Hamsarekha P, Suvarchala S, Yashaswini P, Nousheen S, Mitta SG. Polycystic ovary syndrome-a review. *Int J Emerging Technologies Innovative Res.* 2023;10(11):307-15.
3. Brown EDL, Obeng-Gyasi B, Hall JE, Shekhar S. The Thyroid Hormone Axis and Female Reproduction. *Int J Molecular Sci.* 2023;24(12):e500.
4. Legendre G, Catala L, Morinière C, Lacoëuille C, Boussion F, Sentilhes L, et al. Relationship between

- ovarian cysts and infertility: what surgery and when? *Fertil Steril.* 2014;101(3):608-14.
5. Freytag D, Günther V, Maass N, Alkatout I. Uterine Fibroids and Infertility. *Pathol Molecular Diagnost.* 2021;11(8):10.
 6. Manjula P, Pasham LP, Konatham A, Ravichander T, Tejaswi. Therapeutic goals of terminaton and their efficacy in patients. *Indian J Obstetr Gynecol Res.* 2020;7(4):513-21.
 7. Chauhan S, More A, Chauhan V, Kathane A. Endometriosis: A Review of Clinical Diagnosis, Treatment, and Pathogenesis. *Cureus.* 2022;14(9):e28864.
 8. Ambildhuke K, Pajai S, Chimegave A, Mundhada R, Kabra P. A Review of Tubal Factors Affecting Fertility and its Management. *Cureus.* 2022;14(11):e30990.
 9. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice and Practice Committee. Female age-related fertility decline. *Fertil Steril.* 2014;101(3):633-4.
 10. Dağ ZÖ, Dilbaz B. Impact of obesity on infertility in women. *J Turk-German Gynecolog Assoc.* 2015;16(2):111-7.
 11. Palomba S, Daolio J, Romeo S, Battaglia FA, R Marci, GB La Sala. Lifestyle and fertility: the influence of stress and quality of life on female fertility. *Reproduct Biol Endocrinol.* 2018;16(1):113.
 12. Jaber L, Nashif AS, Diamond G. Consanguinity, Fertility and Reproductive Outcomes: An International Review. *Med Res Arch.* 2023;11(7.1):85-6.
 13. Sutter Health. Female Questionnaire, 2019. Available at: <https://www.sutterhealth.org/pdf/services/fertility/female-fertility-patient-questionnaire-pamf.pdf>. Accessed on 15 June 2024
 14. Idaho Urologic Institute. Infertility Questionnaire, 2010. Available at: <https://www.uslegalforms.com/form-library/469896-infertility-questionnaire-idaho-urologic-institute>. Accessed on 15 June 2024
 15. Mamatha CH, Sreelatha B. A Clinical Study on Factors Influencing Occurrence Infertility in Females. *Int J Pharmaceut Clin Res.* 2024;16(1):1678-83.
 16. Alawan SF, Khamees SS, Tahir SS, El-Deweny GA. Causes of Infertility in Women. *Int Res J Pharmacy Med Sci.* 2020;3(4):5-6.
 17. Shinde KP, Krovi N, Dhutraj PG. Study of factors contributing to female infertility. *Int J Reproduct Contracept Obstetr Gynecol.* 2021;10(7):2591-5.
 18. Deshpande PS, Gupta AS. Causes and prevalence of factors causing infertility in a public health facility. *J Human Reproduct Sci.* 2019;12:287-93.
 19. Baby A, Anila AV, Cindy J, Krishnaveni K, Shanmuga S. A Prospective Evaluation of Causes and Treatment of Infertility in A Tertiary Care Hospital Erode Asian. *J Pharmaceut Clin Res.* 2018;11(2):149-53.

Cite this article as: Thatipelli RC, Parunandi Y, Nousheen S, Shenkeshi S, Fathima H, Anitha A. An observational study on causes of female infertility. *Int J Reprod Contracept Obstet Gynecol* 2024;13:2450-6.