IJPSR (2026), Volume 17, Issue 1 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 04 June 2025; received in revised form, 20 December 2025; accepted, 26 December 2025; published 01 January 2026

EXPLORING THE ETIOLOGY OF FEMALE INFERTILITY IN INDIA: A NATIONWIDE SURVEY ANALYSIS

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Keywords:

Female infertility, Female Reproductive health survey, Epidemiology, Polycystic ovarian syndrome, Expert opinion, tuberculosis

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ABSTRACT: Background: Female infertility is a substantial but sometimes disregarded factor in infertility in couples. The problem is made more difficult to resolve by social shame, cultural hurdles, and a dearth of thorough data on female infertility. **Aims and Objectives:** This study aimed to evaluate the current clinical practices, diagnostic approaches, and management strategies for female infertility among gynaecologists in India. **Materials and Methods:** A comprehensive survey was conducted during the 19th Annual Conference of the Indian Fertility Society (IFS), FERTIVISION-2023. A total of 1039 gynaecologists from various regions of India participated. The survey comprised 11 key questions on various aspects such as the percentage of female patients, common age, most common causes of infertility, prevalence of tubal factors, preferred ovulation induction drug in intrauterine insemination (IUI) cycles, the prevalence of polycystic ovarian syndrome (PCOS), and the preferred methods of ovulation tracking. **Results:** Amongst the participants, 38.80% (n=435) reported that 11-15% of their female patients faced fertility-related issues, the majority of women (39.3%) were in the 25–29 year age group. In our survey, the prevalence of tubal factor infertility was reported to be 5%–10%, with 37.63% respondents. Notably, regional differences were observed, with Northern India reporting the highest prevalence of female infertility. **Conclusion:** The analysis reveals notable differences in how female infertility is diagnosed and treated in various Indian areas. These results highlight the necessity of standardised diagnostic procedures, raised awareness, and thorough training for Indian healthcare professionals.

INTRODUCTION: Infertility affects both men and women and is defined as the inability to conceive a child despite regular, unprotected sexual intercourse over a period of time.

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.17(1).339-45

This article can be accessed online on
www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(1).339-45

According to the World Health Organization [1], the majority of infertile couples worldwide experience primary infertility, wherein the woman has never had a live birth.

However, secondary infertility can occur after a successful first pregnancy, potentially affecting women at any stage of their reproductive lives [2]. Despite its prevalence, infertility has historically received less research attention compared to fertility studies.

The issue gained recognition as a significant health concern during the 1994 International Conference on Population and Development (ICPD) Program of Action in Cairo (UNFPA, 1994). Globally, it is estimated that 50 to 80 million couples experience infertility during their reproductive years [3].

The nature of infertility differs significantly between high-income and low- to middle-income countries. In addition to anatomical, genetic, endocrinological, and immunological factors, a significant proportion of women in developing nations face preventable causes of infertility. These include sexually transmitted diseases (STDs), pelvic inflammatory diseases (PIDs), tubal damage, postpartum infections, post-abortion infections, complications from previous contraceptive use, and polycystic ovarian syndrome (PCOS) [4, 5]. In India, infertility is a growing concern, with an estimated 13 to 19 million couples affected at any given time [6].

Secondary infertility in particular is associated with factors such as early age at first pregnancy, lack of prenatal care during previous pregnancies, unintended pregnancies, stillbirths, postpartum infections, HIV and other sexually transmitted infections (STIs), and other obstetric complications [7]. These findings highlight the urgent need for preventive measures, especially in low-resource settings where STIs and unsafe deliveries contribute to the majority of infertility cases.

Infertility rates exceeding 5% often point to preventable or treatable causes [8]. Therefore, prevention should take precedence over treatment. In developing countries, addressing preventable causes such as infections, unsafe abortions, and complications from deliveries could significantly reduce infertility rates [4]. Against this backdrop, the present study seeks to examine the risk factors associated with infertility among women in Indian districts with high infertility rates. Additionally, it explores treatment-seeking behaviours and the broader impact of infertility on fertility, drawing insights from the most recent national-level data.

MATERIALS AND METHODS: A survey was conducted during the 19th Annual Conference of the Indian Fertility Society (IFS), Fertivision-2023. The survey was moderated by a panel of eminent gynaecologists, including Dr. Kanad D. Nayar, Dr. Surveen Ghumman, Dr. Pankaj Talwar, and Dr. Neena Malhotra, with Dr. M. Venugopal serving as the survey in-charge and Dr. Shalini Chawla Khanna as the survey coordinator. A total of 1,039 gynaecologists participated in the survey, which aimed to assess knowledge regarding primary and secondary causes of female infertility, awareness of fertility preservation techniques, identification of barriers to fertility preservation, and current treatment options.

The questionnaire comprised 11 key questions addressing various aspects such as the percentage of female patients seen by participants, the common age for female infertility, the most common causes of infertility, the prevalence of tubal factors, the incidence of infertility linked to tuberculosis (TB), screening practices for TB, the preferred ovulation induction drug in intrauterine insemination (IUI) cycles, the prevalence of polycystic ovarian syndrome (PCOS), and the preferred methods of ovulation tracking. The questionnaire was developed based on available published data and expert recommendations in the field.

The panel discussed prevalent clinical practices in female fertility care and highlighted the limitations of conventional assisted reproductive technology (ART) based on available evidence and their clinical experience. During the conference, the questionnaires were circulated to participating gynaecologists for discussion and voting to gather their expert opinions. The details of the questions posed, the experts' opinions, and the supporting evidence are summarized below.

In summary, this survey aimed to provide valuable insights into the current landscape of female infertility management among gynaecologists. The findings are expected to facilitate the development of targeted programs to enhance care and counselling for women facing infertility.

RESULTS AND DISCUSSION: A total of 1,039 gynaecologists, representing diverse geographical regions across India including Northern, Southern, Eastern, Western, and Central areas responded to the survey. The regional distribution of respondents was as follows: North (n=334, 29.79%), South

(n=312, 27.83%), East (n=169, 15.08%), West (n=166, 14.81%), and Central (n=140, 12.49%). This geographical diversity ensures a comprehensive representation of perspectives and practices in the field of female infertility management across India. The findings provide valuable insights into current clinical practices and the perspectives of gynaecologists regarding female infertility management in the country. The prevalence of female infertility among Indian couples seeking treatment is estimated to be approximately 11-15%. Studies on infertility often face significant challenges, including variations in the definition of infertility, methodological inconsistencies, and limitations in generating population-based estimates, as highlighted by the World Health Organization (WHO) [9]. To address these complexities and gain a more accurate understanding, the survey explored the percentage of female patients presenting with fertility-related issues in infertility practices. This approach aimed to shed light on the true extent of female infertility cases, which may not be fully reflected in reported statistics. The prevalence of currently infertile women was reported to be 5%, while the percentage of women who had ever experienced primary and secondary infertility was 15% and 3.1%, respectively [10]. The responses from specialists regarding the percentage of female patients presenting with fertility-related issues varied significantly. Among the participants, 38.80% (n=435) reported that 11-15% of their female patients faced fertility-related issues. Meanwhile, 16.32% (n=183) indicated that 16-30% of their patients were affected, and 14.54% (n=163) observed fertility-related issues in more than 30% of their female patients. Additionally, 14.18% (n=159) noted that 6-10% of their patients experienced fertility challenges, while only 3.12% (n=35) reported that less than 5% of their female patients faced such issues. These findings highlight the varying degrees of impact of female infertility across different patient populations and clinical settings **Table 1.** Despite the importance of determining precise rates of female infertility in developing nations, challenges persist due to ambiguities in defining infertility and deficiencies in accurate reporting mechanisms. As a result, existing data may not fully capture the true prevalence of female infertility. However, future research endeavours hold promise in identifying the primary etiological factors contributing to female infertility.

TABLE 1: PERCENTAGE OF FEMALE WITH INFERTILITY RELATED ISSUE

Que 1: What percentage female patients in your practice approach have fertility related issues?		
Answer	**No. of Response**	**% Respondent**
11 to 15%	435	38.80
16 to 30%	183	16.32
>30%	163	14.54
6 to 10%	159	14.18
<5%	35	3.12

In addition to infertility caused by physiological conditions, several preventable factors contribute to its prevalence. These include infections, poor menstrual hygiene, lifestyle factors, advancing maternal age, delayed marriage, postponement of childbearing for over a year, socioeconomic challenges, and occupational hazards [11, 12]. Consequently, this study was designed with the primary objective of estimating the prevalence rate of primary infertility among women of reproductive age. In a related survey, the majority of women (39.3%) were in the 25–29 year age group, followed by 12.6% in the 20–24 year group and 13.6% in the 30–34-year group [13]. The findings of our study align with these results, as presented in **Table 2.**

TABLE 2: COMMON AGE GROUP OF WOMEN APPROACHING FOR INFERTILITY ISSUES

Que 2: What is the common age group of women approaching for infertility issues?		
Answer	**No. of Response**	**% Respondent**
26-30 years	523	46.65
31-35 years	487	43.44
36-40 years	87	7.76
21-25 years	18	1.61
>40 years	5	0.45

To explore further, the next question focused on polycystic ovary syndrome (PCOS), a common condition often linked to infertility in women of childbearing age. This study utilized bibliometric analysis to examine the current research landscape on PCOS and its association with infertility [14]. The prevalence of infertility in women with PCOS is estimated to range between 70% and 80%, while infertility impacts approximately 15% of couples globally. Effective management of female infertility requires a thorough patient history, followed by detailed physical, gynaecological, and endocrine examinations [15]. The aetiology of infertility is typically investigated through various diagnostic tests, including assessments of ovarian function and reserve, evaluations of uterine abnormalities, and tests for tubal permeability. PCOS is recognized as a leading cause of infertility and is one of the most common gynaecological and endocrine disorders, affecting 7% to 15% of women of reproductive age, as shown in **Table 3.**

TABLE 3: COMMON CAUSE FOR INFERTILITY IN WOMEN

Que 3: What is the most common cause of infertility in women?		
Answer	**No. of Response**	**% Respondent**
PCOS	757	67.53
Poor ovarian reserve	134	11.95
Unexplained	79	7.05
Tubal factor	75	6.69
Endometriosis	64	5.71
Uterine factor	11	0.98
Others	1	0.09
Que 4: What is the prevalence of PCOS in infertile women?		
Answer	**No. of Response**	**% Respondent**
11-20%	594	52.99%
21-30%	304	27.12%
5-10%	156	13.92%
>30%	59	5.26%

Approximately 30% of women experience infertility due to fallopian tube disorders, with 10%–25% of these cases attributed to proximal fallopian tube obstruction [14, 16]. The fallopian tube plays a crucial role in facilitating the union of sperm and egg, and its proper functioning is essential for natural conception. Tubal obstruction remains a common cause of infertility, with many patients seeking to unblock their fallopian tubes to restore reproductive function. Accurate diagnosis and effective treatment are critical in managing this condition. In our survey, the prevalence of tubal factor infertility was reported to be 5%–10%, with 37.63% (n=391) of respondents acknowledging its significance, as detailed in **Table 4.**

TABLE 4: PREVALENCE OF TUBAL FACTOR IN INFERTILE FEMALE PATIENTS

Que 5: What is the prevalence of tubal factor in your female patients with infertility		
Answer	**No. of Response**	**% Respondent**
5-10 %	391	37.63
11-20%	301	28.97
Less than 5%	164	15.78
21-35%	130	12.51
Most patients	40	3.85
Never send investigations beyond semen analysis	13	1.25

Diagnosing genital tuberculosis (TB) as a cause of infertility remains a significant challenge for clinicians due to the lack of standardized diagnostic protocols. In low- and middle-income countries (LMICs), tub peritoneal damage is a common cause of infertility, often linked to infectious aetiologies, while anovulation is more prevalent in high-income countries (HICs). Genitourinary TB, a form of extra pulmonary TB (EPTB), accounts for approximately 9% of all EPTB cases globally [17]. Genital TB is a recognized cause of female infertility, resulting from complications such as endometrial injury, tubal obstruction, and involvement of the ovaries and cervix. It is

estimated that genital TB affects 5% of women presenting with infertility in clinics worldwide, with prevalence rates ranging from less than 1% in HICs to 3–26% in LMICs. In India, the annual burden of EPTB is reported to be 20–25%, with 4% of these cases attributed to urogenital TB, encompassing both urinary tract and genital TB. Previous studies have attempted to define genital TB using individual diagnostic criteria, including microbiological testing, ultrasound (USG), and laparohysteroscopy [17]. However, a comprehensive definition incorporating all diagnostic modalities, clinical presentation, USG, laboratory findings, and laparohysteroscopy is not yet available. The complexity of accurately diagnosing genital TB underscores the need for an integrated approach, as highlighted in **Table 5.**

TABLE 5: PREVALENCE OF TB AMONGST WOMEN WHO APPROACH FOR TREATMENT OF INFERTILITY

Que 6: What is the prevalence of TB amongst women who approach for treatment of infertility?		
Answer	**No. of Response**	**% Respondent**
10-20%	368	32.83
5-10%	292	26.05
<5%	229	20.43
20-30%	162	14.45
30-40%	36	3.21
>40%	5	0.45
Que 7: How do you screen your patients for TB?		
Answer	**No. of Response**	**% Respondent**
TB gene expert	408	36.49
Endometrial biopsy- AFB culture and sensitivity	340	30.41
TB PCR	184	16.46
TB Bactec test	99	8.86
No screening	70	6.26
On laparoscopic appearance	17	1.52

Oral ovulogens remain the most commonly utilized intervention in the management of subfertility due to their cost-effectiveness, safety, and ease of administration compared to gonadotropins. The primary oral ovulogens include clomiphene citrate, letrozole, and metformin. Comparative trials have not demonstrated a significant advantage of clomiphene over letrozole, or vice versa, in women with anovulatory polycystic ovary syndrome (PCOS). Both drugs achieve ovulation rates of approximately 70–80% and pregnancy rates per cycle of 20–25% [18]. Clomiphene also plays an important role in mild ovarian stimulation protocols for *in-vitro* fertilization (IVF) due to its ability to prevent premature luteinizing hormone (LH) surges. However, its use is often limited by adverse effects on the endometrium and cervical mucus, which can become resistant with repeated cycles, necessitating alternative therapeutic options. Letrozole, on the other hand, has shown reasonable success in IVF cycles, although its broader application has been hindered by concerns over foetal anomalies. These concerns were based on flawed studies, which led to restrictions on the drug's use in several countries [18]. Metformin, once considered a cornerstone in the treatment of PCOS, is now primarily recommended for specific subsets of patients, including those with glucose intolerance or clomiphene-resistant cases, particularly in obese women. However, its adverse effect profile limits its widespread use. Further research into safer and more effective alternatives, such as orally active gonadotropins, may expand the options for ovulation induction in the future. In our survey, oral ovulogens combined with gonadotropins emerged as the preferred agents for ovulation induction in intrauterine insemination (IUI) cycles, as highlighted in **Table 6.**

TABLE 6: PREFERRED OVULATION INDUCTION DRUG USED IN IUI CYCLES

Ques 8: What is the preferred ovulation induction drug you use in IUI cycles?		
Answer	**No. of Response**	**% Respondent**
Oral ovulogen with gonadotropins	454	40.50
Letrozole	373	33.27
Clomiphene citrate	216	19.27
Gonadotropins	70	6.24
Prefer natural cycle IUI	8	0.71

To conclude the survey, clinicians were asked to specify their region of practice within India. This question was included to address the considerable regional variability in infertility rates across the country. The complexity of infertility patterns in India is further underscored by differences in the prevalence of primary infertility observed among various castes and tribes within the same geographic region. Additionally, cultural stigmas surrounding female infertility and inadequate reporting practices often compromise the accuracy of infertility data, leading to underreporting and misrepresentation of prevalence rates. By gathering information on the practice regions of participating doctors, we aimed to indirectly assess the incidence of female infertility across different parts of India.

Limitations: This survey offers valuable insights into the practices and perspectives of gynaecologists regarding female infertility management in India; however, several limitations must be acknowledged. Firstly, the reliance on self-reported data introduces the possibility of response bias, as participants' answers may have been influenced by personal beliefs, experiences, or the desire to provide socially acceptable responses. Additionally, the survey was conducted among gynaecologists attending a specific conference, which may have excluded perspectives from other relevant specialists, such as reproductive endocrinologists, fertility specialists, and urologists. The design of the questionnaire, including limited response options, may have further influenced participants' answers, potentially restricting the range of insights obtained. Furthermore, the survey's focus on clinicians attending a fertility-focused conference may not fully capture the broader population of gynaecologists practicing across India, limiting the generalizability of the findings. Another limitation is the cross-sectional nature of the survey, which provides a snapshot of current practices and opinions but lacks longitudinal data to assess evolving trends over time. Additionally, the absence of mechanisms to verify or validate the reported practices and beliefs of respondents poses a challenge in confirming the accuracy and reliability of the collected data. Despite these limitations, the survey provides valuable preliminary insights into the landscape of female infertility management in India. It underscores important areas for further research, while highlighting the need for more comprehensive, representative, and longitudinal studies to better understand and address the challenges in this field.

CONCLUSION: In summary, the survey conducted amongst gynaecologists at the Indian Fertility Society's (IFS) 19th Annual Conference provides insight into the state of female infertility diagnosis and treatment in India today. The results underscore the complex issues that patients and healthcare professionals encounter, such as lack of standardised guidelines, cultural stigma, and restricted access to specialised treatment. The survey also identifies areas that might use improvement, including raising awareness, improving training for healthcare professionals, and encouraging studies to learn more about the frequency and causes of female infertility.

ACKNOWLEDGMENT: Authors are thankful to Dr. Vivek Sharma and Dr. Vishal Dave (Intas Pharmaceutical Ltd, Gujarat, India) for critically reviewed the manuscript and fruitful suggestions. Authors also acknowledge Ms. Sakshi Srivastava and Dr. Mehul R. Chorawala, Intas Pharmaceutical Ltd, Gujarat, India for medical writing assistance and additional editorial communication. The authors also grateful to the study patients for their participation in this study.

Author's Contribution: KDY – Conception and designing, Definition of intellectual content, Literature survey, Review questionnaire and manuscript flow and submission of article; Overall Monitoring, Coordination and Subsequent Manuscript Edition/Revision; SGS, VM – Concept, Design, Prepared first draft of manuscript, editing, and manuscript revision, Review Questionnaire; SG, SCK – Design to collect the survey, Questionnaire preparation and Data collection; AS – Review Manuscript and Validation of Questionnaire (QA/QC), Data collection and analysis, Interpretation of Data and preparation of Tables.

Declaration and Statement:

Funding: The author declares that no funds have been received from Government or non-government bodies to conduct this study.

Data Availability Statement: The datasets generated during study are available from corresponding author upon reasonable request.

Declaration of Competing Interest: The author declares that they have no known competing financial and/or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Consent to Participate: All participants provided a written informed consent form to participate in the study.

Consent for Publication: Consent for publication was obtained from all authors, the participants or legally authorized representatives involved in this study.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

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How to cite this article:
Nayar KD, Sindhu SG, Venugopal M, Khanna SC, Gupta S and Sethi A: Exploring the etiology of female infertility in India: a nationwide survey analysis. Int J Pharm Sci & Res 2026; 17(1): 339-45. doi: 10.13040/IJPSR.0975-8232.17(1).339-45.