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Etiology of Primary Subfertility in Women Presenting to Tertiary Care Hospital

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ABSTRACT

Introduction: Failure to conceive after one year of regular unprotected intercourse is a common and agonising event in young women of childbearing age and is referred to as primary subfertility. The causes are diverse and they include ovulatory dysfunction and tubal disease, endometriosis, uterine anomalies and infertility. **Objective**: To determine etiological factors of primary subfertility in women attending a tertiary care hospital. **Material and Methods**: A descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, Civil Hospital Karachi, Pakistan from April, 2024 to September, 2024. One hundred and sixty women between 18 and 40 years of age with primary subfertility were recruited using non-probability consecutive sampling. Etiological factors were identified through a detailed history, clinical examination, hormonal evaluation, ultrasound, hysterosalpingography, and diagnostic laparoscopy. Descriptive statistics were calculated to analyse the data. **Results**: The prevalent cause was ovulatory dysfunction (35.6 per cent), followed by tubal factor infertility (26.3 per cent), unexplained infertility (15.6 per cent), endometriosis (12.5 per cent), and uterine abnormalities (10.0 per cent). Abnormalities in the hormones were high LH (22.5%), thyroid dysfunction (11.3%), hyperprolactinemia (8.1%), and high FSH (6.3%). **Conclusion**: Tubal factors and ovulatory disturbance continue to be the commonest etiologies of primary subfertility. A complete and early assessment with minimally invasive laparoscopy is necessary to maximise the chances of diagnosis and enhance reproductive outcomes.

INTRODUCTION

The inability to conceive after at least one year of regular unprotected sex is a huge reproductive and health concern all over the world known as primary subfertility. Its frequencies are between 10 and 15 percent world wide, and even higher in the South Asian nations as a result of late detection, lack of assisted reproductive centers and elevated pelvic infection mass. Primary subfertility is multifactorial in its causes and this can be attributed to ovulatory dysfunction, tubal occlusion, pelvic adhesions, endometriosis, and abnormalities of the uterus. In this respect, diagnosing such etiologies in tertiary care hospitals is focused on surgical assessment, where a lack of evidence on imaging results is common (1). Minimally invasive processes have proved to be more successful in the non-gynecological surgical research. As an example, Quah et al. pointed out that laparoscopic appendectomy proved to be better than open surgery in complicated appendicitis because it resulted in lower morbidity and more rapid recovery. Likewise, Lee et al. in a meta-analysis of pregnant patients mentioned the superior safety outcomes of laparoscopy compared to open surgery in vulnerable populations as well (2).

The findings support a wider clinical significance of laparoscopy in women of reproductive years in need of fertility assessment. Comparative surgical studies- Evidence of comparative surgical studies compounds a strong case in support of prioritizing laparoscopy in the diagnosis and medical conditions that lead to subfertility. Ibraheem et al. has shown the general benefits of laparoscopic surgery on the decrease in complications rates and the stay of the patient in the hospital when compared to the open position (3). Basukala et al. also established that laparoscopic processes are less morbid and offer improved conversion to normal activity than open surgery in a more recent retrospective cohort (4). This evidence is very pertinent in the treatment of subfertile women with tubal or peritoneal factors, where minimisation of surgical trauma and formation of adhesions is essential to the maintenance of fertility potential. Similarly, meta-analysis reviews, such as the one by Poprom et al., have consistently found that postoperative complications are fewer after laparoscopic treatment than after open surgery (5).

There is an increased demand for a minimally invasive approach, especially in complex presentations.

Subramaniam demonstrated that patients undergoing laparoscopic surgery recovered more quickly and experienced a better quality of life, in addition to benefiting more than those who received open surgery (6). Takami et al. also supported the claim by reporting positive results for patients with complicated appendicitis who underwent laparoscopic treatment compared to those treated with open approaches (7). Applying these results to everyday gynecologic practice, women who undergo laparoscopic adhesiolysis or tuboplasty obtain the advantages of lower adhesion recurrence and quicker recovery, which eventually lead to enhanced reproductive outcomes. Moreover, Hussein et al. emphasised that even obese patients, typically contributing to greater surgical risks, reported much improved postoperative recovery and quality of life with laparoscopic activity compared with open surgery procedures (8).

Pelvic aspects, such as pelvic inflammatory disease or endometriosis, can be compared with surgery experiences in complicated appendicitis. Nazir et al. demonstrated that laparoscopic appendectomy has lower complication rates compared to the open method for perforated appendicitis (9). Srivastava also confirmed the findings that laparoscopic surgery has generally improved clinical outcomes compared to open surgery (10). These results are reflective of the gynaecological scenario, where laparoscopic intervention in severe pelvic disease has a direct impact on diagnosis, surgery, and conception success. Similarly, Nascimento et al. emphasised the cost-effectiveness of laparoscopic procedures in public health systems, alongside stating not only clinical but also economic benefits of laparoscopic approaches to open methods (11). These findings are essential in resource-limited tertiary care hospitals where cost is a significant factor that determines access to services for women with subfertility. Minimal invasive surgery also benefits children and young women disproportionately. Pogorelic et al. found better results for laparoscopic appendectomy compared to open procedures in the pediatric population, with fewer complications and a shorter recovery time (12).

Similarly, Bhuiyan et al. conducted a study in a South Asian tertiary hospital, where laparoscopic procedures were also found to be more favourable in terms of overall outcomes than the open approach (13). These lessons apply to young subfertile women, whose fertility preservation is of primary concern, and the trauma of surgery should be limited. Becker et al. further contributed to this observation by comparing laparoscopic and robotic experiences, indicating that, in general, minimally invasive approaches, whether laparoscopic or robotic, have a definite benefit in shortening hospital stays and augmenting recovery patterns (14). Different special populations, like the geriatric or the overweight patients, have also been investigated, and their results always tend to be in favour of the laparoscopic approach. Wang et al. demonstrated that laparoscopy, when performed on elderly patients, resulted in fewer complications compared to open appendectomy (15). Ertekin also pointed out an increase in the quality of life of the overweight and obese patients treated laparoscopically (16).

The relevance of these findings includes improvements in surgical techniques in which subfertility in women of advanced reproductive age is commonly presented and when proper surgical intervention is needed to facilitate an appropriate balance between the benefits of such investigations and the least morbidity of the patient after the procedure. Monrabal Lezama et al. identified conversions of laparoscopic surgery to open surgery as an outcome predictor that requires minimally invasive, successful procedures initially (17). Lastly, the wound healing and infection control role is a vital determinant in the circumstances under which subfertile women can use surgical intervention. Khadilkar et al. reported improved perioperative outcomes with laparoscopic as compared to open treatment in a large patient population series (18). Guler et al. further demonstrated that the wound infection rate and healing time after laparoscopic and open surgery for complicated appendicitis were significantly decreased and faster, respectively (19). These findings endorse the minimally invasive approaches in tertiary health facilities that handle primary subfertility as the leading causes of tubal factors of infertile couples are pelvic infection and adhesion.

The ovulatory, tubal, peritoneal, uterine, and unexplained causes of primary subfertility are its direct etiologies. Comparative surgical studies strongly support laparoscopic techniques as the most favoured approach to such surgery over open surgery in assessing and treating such gynaecological problems (14). In the many cohorts of pregnant women, obese patients, and elderly and pediatric patients, laparoscopy has remained safer, more effective, and cost-efficient. Translating these lessons to reproductive health, evaluation of tubal block, endometriosis or adhesions by minimally invasive surgery, specifically diagnostic laparoscopy, should be prioritised in women diagnosed with primary subfertility in tertiary hospitals (12). This would not only result in a precise diagnosis but also bring about better reproductive outcomes, less morbidity, and rapid recovery.

Objective

To establish the etiological factors underlying primary subfertility in women attending a tertiary care hospital, and evaluate reproductive, anatomical, endocrinological, and pathological causes, to base the successful clinical management approach on them.

MATERIALS AND METHODS

Study Design: Descriptive cross-sectional study

Study Setting: Department of Obstetrics and Gynaecology, Civil Hospital Karachi, Pakistan

Duration of the Study: From April, 2024 to September, 2024.

Inclusion Criteria

It included women between 18 and 40 years, who have primary subfertility, i.e. failure to conceive after at least 12 months of regular unprotected intercourse. The subjects were required to be fertility treatment-free.

Exclusion Criteria

Patients with secondary subfertility, previous pelvic intervention, hysterectomy, history of known male factor

infertility, systemic diseases interacting with fertility, or refusal to sign an informed consent were excluded.

Method

Informed consent was acquired and all those meeting the inclusion criteria were enrolled. Detailed history was taken with information on the characteristics of the menstrual cycle, previous medical and surgical history, past family history of infertility and lifestyle. General physical assessment, measurement of body mass index, and focused gynaecological assessment were performed clinically. Hormonal evaluations, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and prolactin, were conducted in the laboratory. Assessment of uterine morphology, ovarian reserve and polycystic ovarian syndrome was done by trans vaginal ultrasound. Hysterosalpingography (HSG) and diagnostic laparoscopy were used as diagnostic tools to confirm suspected tubal and peritoneal factors. Semen parameters were checked, and males were excluded if they had a male factor of infertility. All the findings were meticulously recorded on a pro forma. The information was typed, coded and analysed to determine the proportion and distribution of different etiological factors in the study population about primary subfertility.

RESULTS

The study included 160 women with primary subfertility. The total sample mean age was 29.8 % 4.5 years, with most of them falling in the age range of 26-30 years. The average duration of marriage was 6.2 ± 2.8 years. The majority of the women (48.1%) possessed a normal body mass index, 34.4% were overweight, and 17.5% were obese.

Table 1

Demographic Characteristics of Study Participants (n=160)

Variable	Mean ± SD / Frequency (%)
Age (years)	29.8 ± 4.5
Duration of marriage (years)	6.2 ± 2.8
BMI (Normal)	77 (48.1%)
BMI (Overweight)	55 (34.4%)
BMI (Obese)	28 (17.5%)

Among etiological factors, the most widespread cause of subfertility was discovered to be ovulatory dysfunction at 35.6 percent of women, then tubal factors 26.3 per cent and endometriosis 12.5 percent. 10.0 percent of the cases involved uterine abnormalities (i.e., fibroids and septa), whereas the group of patients with unexplained infertility was 15.6%.

Table 2

Distribution of Etiological Factors of Primary Subfertility (n=160)

Etiological Factor	Frequency (%)
Ovulatory dysfunction	57 (35.6%)
Tubal factor	42 (26.3%)
Endometriosis	20 (12.5%)
Uterine abnormalities	16 (10.0%)
Unexplained infertility	25 (15.6%)

Hormonal testing showed that 22.5 per cent of them had a high luteinizing hormone (LH), which is indicative of polycystic ovarian syndrome (PCOS). Eleven per cent of respondents had thyroid dysfunction, and 8.1 per cent had hyperprolactinemia. Abnormal FSH levels of <6.3, reflecting reduced ovarian reserve, were found in 6.3%.

Table 3

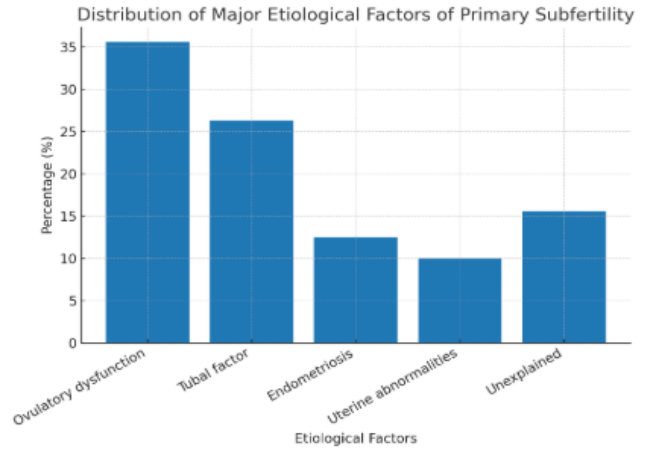
Hormonal Abnormalities among Study Participants (n=160)

Hormonal Parameter	Abnormal Frequency (%)
Elevated LH	36 (22.5%)
Thyroid dysfunction	18 (11.3%)
Hyperprolactinemia	13 (8.1%)
Elevated FSH	10 (6.3%)

The general pattern of etiological factors is described in Graph 1 with ovulatory dysfunction and tubal disease being the primary factors of influence.

Graph 1

Distribution of Major Etiological Factors of Primary Subfertility



DISCUSSION

Etiological spectrum of primary subfertility among women attending a tertiary care centre was investigated in the present study, which revealed ovulatory dysfunction as the most frequent factor, followed by tubal pathology, unexplained infertility, endometriosis and uterine abnormalities (1). These results are in agreement with previously published reports worldwide and regionally, in which ovulatory disturbances (especially polycystic ovarian syndrome (PCOS)) have become one of the leading causes of primary infertility. The epidemiology of tubal factor infertility also indicates the persistence of the burden of pelvic inflammatory disease and post-infectious sequelae in the developing world. The results obtained can be viewed through the lens of surgical investigations comparing open and laparoscopic procedures, which have provided indirect guidance in the management of infertility. Quah et al. showed that the laparoscopic approach to appendectomy in the case of complicated appendicitis allowed both reducing the time of recovery and the number of postoperative complications in comparison to open surgery (2).

Similarly, Lee et al., in their meta-analysis of pregnant women, found that laparotomy during appendectomy is associated with enhanced safety compared to laparoscopy. This evidence highlights the importance of laparoscopy in reproductive medicine, where diagnostic laparoscopy is

the gold standard for assessing the causes of tubal and peritoneal infertility. In our study, close to 26.3 per cent of the ladies had tubal ligation. It is consistent with the literature that claims that minimally invasive evaluation results in better diagnostic yield than traditional imaging. Ibraheem et al. discovered that laparoscopic methods decrease the frequency of complications compared to open procedures, highlighting the safety and efficiency of minimally invasive examination (3). This trend was also validated by Basukala et al., who conducted a retrospective study showing that laparoscopic surgeries had a better outcome compared to open surgeries (4). In their umbrella review, Poprom et al. found that laparoscopy consistently decreased postoperative complications when compared with open surgery (5).

All of these indicate increased utilisation of laparoscopic evaluation in women with suspected tubal pathology. The frequency of endometriosis-caused subfertility in our cohort was 12.5%, which is similar to data obtained at the international scale, indicating endometriosis as a significant cause of infertility. Subramaniam emphasised the point that laparoscopic surgery maintains quality of life, and recovery rates are quicker compared to open procedures (6). Takami et al. reported good results whenever laparoscopy was used in complicated surgical cases (7). Laparoscopy in the context of endometriosis is both diagnostic and therapeutic, as lesion excision or ablation can be achieved, which also promotes fertility. Hussein et al. also showed that the obese patient treated under the laparoscopic method had better recovery and quality of life (8), which applies to PCOS-related infertile women with obesity as a frequent comorbidity. The value of reduced procedures in complex situations is further enhanced by Nazir et al., who concluded that laparoscopy is superior to open appendectomy in the treatment of perforated appendicitis (9). Laparoscopic approaches were also reported to have better results by Srivastava (10).

The results are comparable to those in gynecologic practice, where women with severe pelvic adhesions are better served with adhesiolysis performed laparoscopically, rather than through open techniques. Moreover, in the context of infertility care, cost-effectiveness is significant, especially in cases where resources are limited. Nascimento et al. observed that laparoscopic appendectomy was cost-effective compared to open appendectomy among government-controlled systems (11). In the assessment of subfertility, laparoscopy is a cost-effective approach because it offers both diagnosis and treatment in a single setting. Unexplained infertility, which was encountered in 15.6% of our patients, continues to be a diagnostic problem. Pogorelic et al. established results showing that laparoscopic methods yielded better outcomes in a retrospective study population of pediatric patients (12). Bhuiyan et al. concluded the same trial in a tertiary care hospital setting (13). These observations suggest that, despite the limitations of imaging and laboratory workup in detecting causes, diagnostic laparoscopy may theoretically yield precise results in the form of subtle peritoneal/tubal abnormalities that would otherwise not have been identified.

Becker et al. compared laparoscopic and robotic appendectomies and found that minimally invasive surgery had overall superiority (14). This aims to justify the further development of surgical technology in infertility workups. Subfertile advanced-reproductive-age females are encountered more often, and their surgical management has to optimise risk and diagnostics. Wang et al. established that laparoscopy procedure is safer in elderly patients than open surgery (15). Ertekin documented that laparoscopic operations employed in overweight and obese individuals lead to a better quality of life (16). These results apply to the matter of infertility treatment because not only old age, but also obesity is a significant source of bad reproductive conditions. Monrabal Lezama et al. showed that the conversions of laparoscopic to open surgery were associated with worse results (17). This observation indicates the underlying essence of surgical skill during infertility assessments to reduce excessive complications. Lastly, uterine lesions were responsible for 10 per cent of subfertility in this research.

There is a belief that minimally invasive approaches have better perioperative outcomes compared to open ones. Laparoscopic procedures have also been shown to yield good results in large patient groups by Khadilkar et al. (18), in addition to Gulfer et al., who demonstrated decreased wound infection rates and faster healing rates in laparoscopy compared to open surgery (19). In women who have uterine anomalies that should be surgically corrected, minimally invasive methods lead to improved preservation of reproduction. Generally, the research reveals that ovulatory dysfunction and tubal ligation are the most common causes of primary subfertility. However, the importance of endometriosis, the pathology of the uterus and unexplained infertility cannot be underestimated (16). This congruity in the evidence provided in the surgical literature substantiates the use of laparoscopy as a tool of higher calibre of diagnosis and treatment in reproductive-aged women. The advantage of our research is that it utilises a hospital-based cohort, offering direct clinical applicability to tertiary care practice.

CONCLUSION

The study reveals that the major aetiology of primary subfertility in women attending the tertiary care hospital was ovulatory dysfunction, tubal factor infertility, unexplained infertility, endometriosis and uterine abnormalities. These results agree with regional and international data and support the theory of multifactorial etiology of female subfertility. Hormonal imbalances, especially high LH levels, thyroid dysfunction and hyperprolactinemia, also played a significant role, which further proves the necessity of a thorough endocrine study. Comparative surgery literature also provides support for the hypothesis that minimally invasive laparoscopy is superior to other modalities as a diagnostic and therapeutic tool, with evident advantages in safety, cost-efficiency, and recovery. The introduction of early laparoscopic assessment in the workup of infertility may be a solution to shorten the diagnostic duration and enhance outcomes in a resource-limited setting like

Pakistan. In general, early multidisciplinary interventions are necessary to treat the etiological spectrum, improve the fertility prognosis and reduce the psychosocial impact of subfertility.

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