



# Risk Factors and Clinical Patterns of Infertility in Couples: A Hospital-based Cross-sectional Study in Southern Khyber Pakhtunkhwa, Pakistan

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**Abstract:** Infertility is ranked as the fifth-leading cause of disability in the world's population under 60 years old, according to the World Health Organization, affecting an estimated 80 million people worldwide. This reproductive health disorder can be caused by various factors, including structural, biological, and congenital issues, as well as acquired and environmental variables. To investigate the prevalence and potential risk factors of infertility, a hospital-based cross-sectional study was conducted in district Kohat, Pakistan, from January to May 2021. A total of 120 infertile couples were recruited from the outpatient center at Liaquat Memorial Hospital, and their medical files were reviewed, followed by face-to-face interviews with both partners of each couple. Of the participants, 47.5% were suffering from primary infertility, while 52.5% were affected by secondary infertility. Female infertility was the most common form of infertility, affecting 49.16% of couples, followed by male infertility (15.83%), couples with both partners facing infertility issues (8.33%), and unspecified infertility (26.66%). The most frequent causes of male and female infertility were erection issues (48.27%) and menstrual disorders (44.92%), respectively. Additionally, 46.34% of couples reported stress and anxiety, and 14.16% had a history of assisted reproductive technology. Furthermore, 18.3% of couples had a family history of infertility, with 77.27% of those affected being infertile females. Infertile couples were also assessed based on potential risk factors, including age difference, age at menarche, occupation, smoking, and Body Mass Index (BMI). These findings may aid in identifying the factors contributing to infertility among the population.

**Keywords:** Cross-sectional Study, Infertility, Risk Factors, Clinical Patterns, Reproductive Health Disorder.

## 1. INTRODUCTION

Infertility is the incapability to conceive after trying for one year without the use of contraceptive methods while having normal sexual intercourse [1]. Infertility is the fifth-leading cause of disability in the world's population under 60 years old, according to the World Health Organization. An

estimated 80 million people worldwide are affected severely by the reproductive health disorder of infertility [2]. The frequency of infertility in Pakistan is 22% where, primary infertility is 4% and secondary infertility is 18.0% [3]. Primary infertility is a condition where a couple cannot get pregnancy after 1 year of unprotected sexual intercourse. Secondary infertility is the condition where a couple has perceived previously but became

unable then [4]. Numerous causes of infertility have been reported in studies on different populations, including structural, biological, and congenital factors. Additionally, a number of acquired and environmental variables can affect fertility and cause infertility. The most frequent causes of reproductive impairment include uterine problems, menstrual and ovulation disorders, and irregular menses. The causes of infertility and their patterns of occurrence vary greatly across geographical areas. This discrepancy results from the presence of changing environmental factors that are connected to reproductive activities, such as altering lifestyle and dietary patterns, environmental pollution, age at marriage, and smoking and drinking habits [5]. Deficits in spermatogenesis or sperm transport are the main causes of male infertility. Analysis can be confirmed by doing a complete assessment of semen analyses, gonadotropin and other tests [6]. Infections like gonorrhea and sexually transmitted illnesses used to be the main reasons of infertility, but today stress, male factor, etc. have taken their place. Additionally, it has been demonstrated that the problem of infertility is exacerbated by the rising frequency of lifestyle problems like obesity and addiction in young people as well as medical conditions like diabetes, hypertension, and hypothyroidism [7].

While infertility encompasses various factors, male infertility, particularly in the form of azoospermia, emerges as a significant concern, with non-obstructive azoospermia (NOA) representing the most severe manifestation of spermatogenic failure. Recent genetic investigations have identified specific variants in KCTD19, a gene associated with potassium channel tetramerization, in both Chinese and Pakistani populations experiencing NOA [8]. Couples who struggle with infertility often feel distressed because of societal norms and religious beliefs that may view infertility as a sign of failure on a social, emotional, interpersonal, or personal level [9]. As a result, infertility is not only a medical problem but also has a significant psychological impact and social shame [10]. To date, no studies have provided local estimates of primary and secondary infertility prevalence in District Kohat of the Khyber Pakhtunkhwa province. Therefore, the current study aims to evaluate the clinical patterns and distribution of infertile couples based on potential risk factors in this region.

## 2. MATERIALS AND METHODS

### 2.1 Study Area and Study Design

A cross-sectional study was conducted between November 2020 and April 2021, on a conveniently selected adult population, recruited from the outpatient center at Liaquat Memorial Hospital, a tertiary care hospital in district Kohat, of southern Khyber Pakhtunkhwa. Kohat is a medium sized district located at a distance of about 47 km from Peshawar, the capital of Khyber Pakhtunkhwa, located at 33°35'13N 71°26'29E with an altitude of 489 m (1607 feet) with total area is 2973 km<sup>2</sup> with total population of 7, 82,070 and annual growth rate of 3.25% [11]. Using a convenience sampling technique, 120 participants were enlisted after providing written, reliable, and informed permission. The study included married couples who had been together for more than a year and who did not take contraceptives in situations of primary or secondary infertility. The couple's ages ranged from 19 to 59. Participants from lower socioeconomic classes are more likely to use public hospitals for treatment than couples in middle- to higher-socioeconomic classes, who often choose private hospitals. The information was evaluated and retrieved from the medical records of infertile couples. Age, infertility type, duration, and factors thought to be contributing to infertility were among the details taken from the records. The online questionnaire was sent to infertile couples, and researchers also visited their homes to ensure complete questionnaire responses. Couples in which one partner was reluctant to undergo clinical assessment were excluded from the study.

### 2.2 Questionnaire Designing and Data Collection

In the study, data was gathered through face-to-face interview, using self-generated standardized questionnaire. To ensure conceptual coherence, the questionnaire was first written in English, then translated into the regional tongue (Pashto), and then back into English. Data for this study were gathered using a standardized four-section questionnaire. The participants' age, gender, occupation, and Body Mass Index (BMI) were all covered in the first section's socio-demographic questions. The patients' menstrual histories are covered in the second section. The third section

includes the patients’ medical histories, including information on endometriosis, polycystic ovary syndrome (PCOS), hormonal imbalance, pelvic infection, semen analysis, undescended testicles, issues related to infertility, and treatment guidelines. The fourth part consist of social history and family history of infertile couple such as Cystic Fibrosis and hormone Imbalance.

**2.3 Data Analysis**

Data were managed in Microsoft Excel and descriptive statistics were performed using IBM SPSS Statistics (Version 23). The results were presented in form of tables and graphs to illustrate the distribution through numerical counts and percentages.

**3. RESULTS**

A cross-sectional study was conducted between November 2020 and April 2021 on a conveniently selected adult population of District Kohat in the Khyber Pakhtunkhwa province of Pakistan, with a sample of 120 infertile couples. Questionnaires were filled out by the infertile couples, which included questions related to various risk factors. For convenience, the results were divided into six sections. The first section consists of the types of infertility. The second section consists the demographic and socio-economic factors including age, BMI, family status and occupation. The third section of results is about the distribution of affected

individuals on the basis of potential risk factors. The fourth section consist of disease associated with infertility. The fifth section consist of tendency of couple for assisted reproductive technology. Finally, the sixth section of the results is about the family history of infertility and disease associated with infertility.

**3.1 Types of Infertility in Couples**

A total of 120 couples were analyzed, and they were split into four standard groups: (a) Female affected (b) Male affected (c) Both affected (d) Unexplained infertility. Of the 120 couples studied, 19 (15.83%) were ‘male affected’ couples, bearing primary (63.1%) and secondary (36.8%) type of infertility, 59 (49.16%) were ‘female affected’ couples, bearing primary (28.8%) and secondary (71.1%) type of infertility. 10 (8.33%) were ‘Both’, both partners were affected, with 60% and 40% cases of primary and secondary types of infertility, respectively. Similarly, out of 32 (26.66%) Unexplained couples, no partner specified as infertile, 22 (68.75%) cases were affected with primary and 10 (31.25%) and were affected with secondary infertility (Figure 1).

**3.2 Demographic and Socio-economic Factors of Infertile Couples**

The socio-demographic characteristics of the participants are presented in Table 1. Among 69 affected females, women under age of 25 were 10 (14.49%), ranging 25-35 were 40 (57.97%) and ranging 36-45 were 19 (27.53%). Among 29

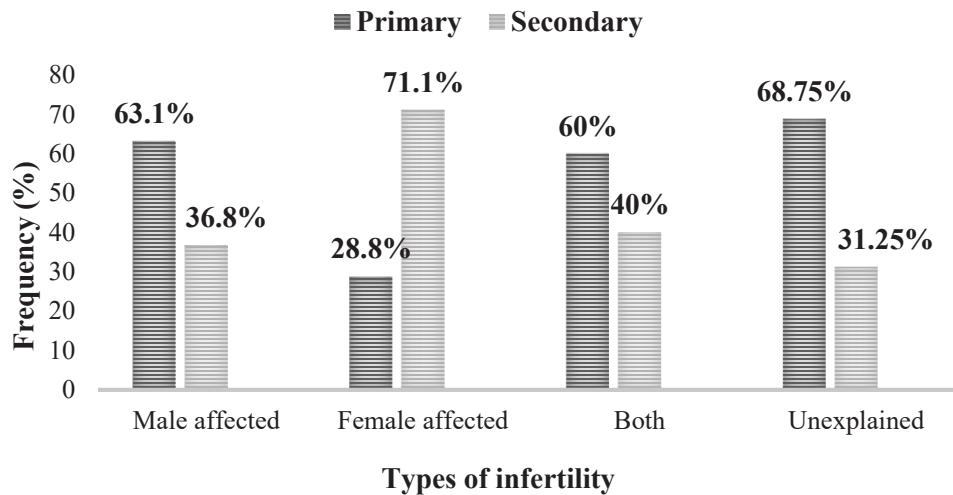


Fig. 1. Types of infertility in couples participated in the study (N = 120).

**Table 1.** Demographic and socio-economic factors of infertile couples in the study (N = 120).

S. No.	Demographic variables	Categories	N	(%)	
1	Women's age	<25 years old	10	14.49	
		25-35 years old	40	57.97	
		36-45 years old	19	27.53	
2	Husband's age	< 25 years old	4	13.79	
		25-35 years old	10	34.48	
		36-45 years old	6	20.68	
		46-56 years old	9	31.03	
3	Couple's age difference	< 1 year	2	1.66	
		1-5 years	73	60.83	
		6-10 years	26	21.66	
		>10 years	19	15.83	
4	'Female Affected' Occupation	Housewife	45	76.27	
		Teachers	5	8.47	
		Medical profession	5	8.47	
		Any other	4	6.77	
5	'Male Affected' Occupation	Govt. employee	2	10.52	
		Teachers	2	10.52	
		Labor	5	26.31	
		Any other	10	52.63	
6	'Both' Occupation	Male	Teacher	2	20.00
			Any other	8	80.00
		Female	Teacher	3	30.00
			Housewife	7	70.00
7	'Unexplained' Occupation	Male	Medical	7	21.87
			Farmer	4	12.5
			Labor	3	9.37
			Teachers	3	9.37
			Govt. employee	3	9.37
		Female	Others	2	6.25
			Unemployed	10	31.2
			Housewife	26	81.2
			Teachers	4	12.5
			Medical	2	6.25
8	Family status (Per month income)	Poor (< Rs. 5000/adult)	14	11.6	
		Low (Rs. 5000 – 10000/adult)	24	20.0	
		Middle (Rs. 10000-20000/adult)	70	58.3	
		High (>Rs. 20000/adult)	12	10.0	

affected males, men under the age of 25 years were 4 (13.79%), between 25-35 years were 10 (34.48%), between 36-45 years were 6 (20.68%) and between 45-56 years of age were 9 (31.03%). On the basis of age difference between partners in a couple, the infertile couples (N=120) were categorized into four groups with age less than one year (1.66%), one to five years (60.83%), and six to ten years (21.66%) and more than 10 years of age were 15.83%. On the basis of occupation, the infertile couples were categorized into four groups, i.e., females affected, 45 (76.27%) women were housewives, 5 (8.47%) were teachers, 5 (8.47%) were having medical profession, and 4 (6.77%) were belonging to other profession. In male affected couples 2 (10.52%) were government employee, 2 (10.52%) were teachers, 5 (26.31%) labor, 11 (57.89%) were having other profession. In couples with both partners affected, 2 (20%) man were teachers, 8 (80%) were having others profession and in 3 (30%) women were teachers and 7 (70%) were housewives. In Unexplained infertile couples, 7 (21.87%) males were associated with medical profession, farmers 4 (12.5%), labors 3 (9.37%), teachers 3 (9.37%), government employees 3 (9.37%), other professions 2 (6.25%), and unemployed 10 (31.2%). In unexplained infertile females 26 (81.2%) were housewives, 4 (12.5%) teachers and 2 (6.25%) were having medical profession. The financial status of the infertile couples was categorized into four groups: poor, low, middle, and high. The majority of cases belonged to the middle-class category in terms of family income.

### 3.3 Distribution of Affected Individuals on the basis of Potential Risk Factors

The female BMI index or status, was determined in which 11 (15.94%) are normal females, 26 (37.68%) were over weighted and 22 (31.88%) were obese. In males 4 (21.05%) are normal, 10 (52.63%) were over weighted and 5 (26.31%) were obese. In Both cases 2 (20%) are normal couples, 5 (50%) were over weighted and 3 (30%) were obese. In unexplained 5 (15.62 %) are normal couples 17 (53.12%) were over weighted and 10 (31.25%) were obese. 7.5% of the respondents had a history of smoking as well. The history of addiction was also reported by male, a total of 16 respondents (13.3%), including Naswar and Hashish, which was

identified as the most popular substance utilized whereas little to no drug usage was observed in women. (Table 2).

### 3.4 Midwifery Variables in Couples

Table 3 shows the duration of infertility and the age at menarche. The majority (43.8%) of couples had primary infertility of 3-5 years' duration and 34.9% of couples had secondary infertility of 4-5 years' duration.

### 3.5 Distribution of Couples with respect to Clinical Factors Associated with Infertility

Figure 2 shows the distributions of infertile females (N = 69) with respect to female factors. Analyzing the female factors in detail where it was responsible for infertility, it was found that the main causes originate in our study population were the Menstrual disorders (44.92%) and Hormonal imbalance (40.57%). Other causes of female infertility included endometriosis (5.79%), Ovarian cyst (1.44%), Uterine cyst (4.34%), PCOS (24.63%), and Fallopian tube blockage (8.69%). Figure 3 shows the occurrence of menstrual disorders in affected females (N = 69) among the infertile couples. The occurrence of menstrual diseases in affected females were as follow: Menorrhagia (18.44%), Dysmenorrhea (51.43%), Oligomenorrhea (21.35%), and Metrorrhagia (8.73%). Figure 4 shows the distributions of infertile males (N = 29) with respect to male specific clinical factors. Male infertility was most frequently caused by erection problems (48.27%) and ejaculatory problems (27.58%). The most often diagnosed instances, according to the findings of the semen analysis, were Azoospermia (17.24%), Asthenospermia (3.44%), Payospermia (6.89%), Hematospermia (3.44%), Oligospermia (10.34%), Teratozoospermia (3.44%) respectively. There were two cases of undescended testicle (10.34%).

### 3.6 Associated Diseases, may Influence Fertility, in the Infertile Couples

Data were collected from infertile couples regarding various chronic diseases. Out of 120 affected couples, 82 reported having a chronic medical condition in either male, female or both partners. The results showed highest frequency of



**Table 2.** Potential risk factors in infertile individuals in couples (N = 120).

S. No.	Variables	Categories	N	(%)
1	'Male affected' BMI status	Normal	4	21.05
		Overweight	10	52.63
		Obese	5	26.31
2	'Female affected' BMI Status	Normal	11	15.94
		Overweight	26	37.68
		Obese	22	31.88
3	'Both' BMI status	Normal	2	20.0
		Overweight	5	50.0
		Obese	3	30.0
4	'Unexplained' BMI status	Normal	5	15.62
		Overweight	17	53.12
		Obese	10	31.25
5	History of Miscarriage	Yes	31	25.8
		No	89	74.2
6	Number of miscarriages (n=31)	Once	20	64.5
		Twice	4	3.33
		3 times and more	7	5.83
7	History of smoking	Yes	9	7.5
		No	111	92.5
8	History of drug addiction	Yes	16	13.3
		No	104	86.6
9	Tea or coffee per day	1 cup	16	13.3
		2 cup	45	37.5
		3 cup	35	29.1
		4 cup and more	24	20.0

**Table 3.** Midwifery variables of infertile couples (N = 120).

S. No.	Variables	Categories	N	(%)
1	Duration of primary infertility	2 years	13	22.8
		3-5 years	25	43.8
		5-10 years	14	24.5
		>10 years	5	8.7
2	Duration of secondary infertility	2 years	3	4.7
		3 years	14	22.2
		4-5 years	22	34.9
		5-10 years	19	30.1
3	Age at menarche	>10 years	5	7.9
		Early ( $\leq 11$ years)	25	20.83
		Normal (12-14years)	87	72.5
		Late ( $\geq 15$ years)	8	6.66

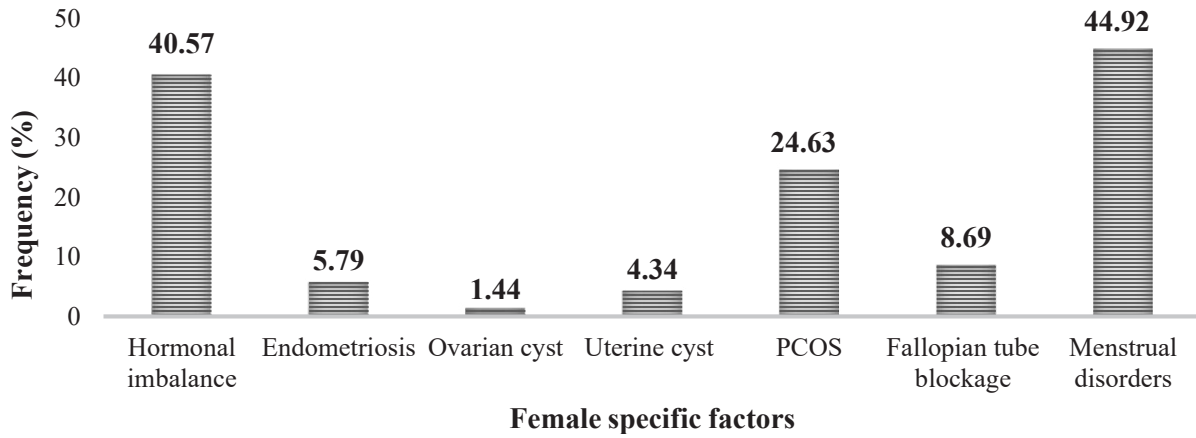


Fig. 2. Distribution of infertile females with respect to occurrence of clinical conditions (N = 69).

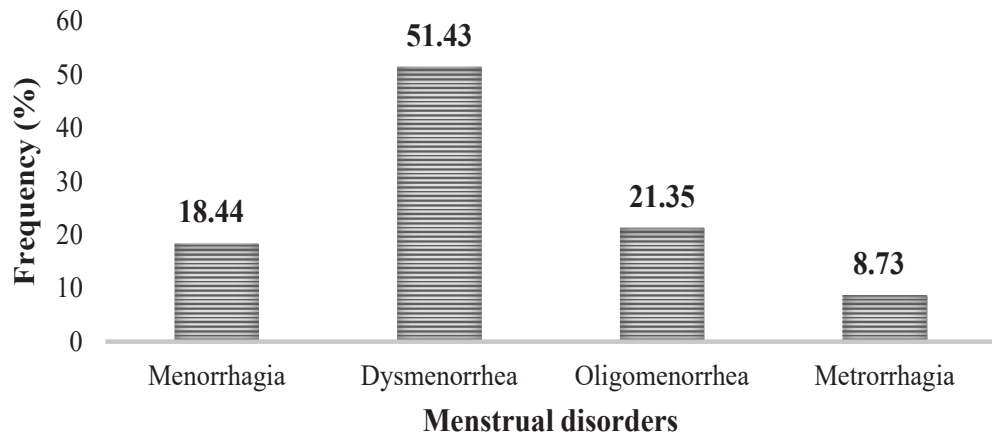


Fig. 3. Distribution of menstrual disorders on the basis of its type (N = 31).

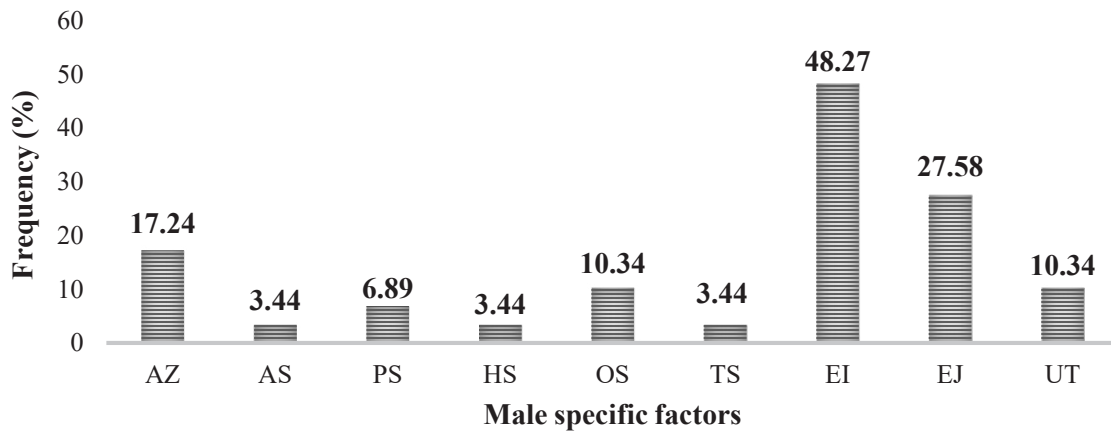


Fig. 4. Male specific clinical factors in infertile males (N = 29).

AZ= Azoospermia, AS=Asthenospermia, PS=Payospermia, HS=Hemospermia, OS=Oligospermia, TS=Teratozoospermia, EI=Erection Issue, EJ=Ejaculatory Issue, UT=Undescended testicle.

stress in infertile couples (46.34%), followed by high blood pressure (14.63%), Diabetes (12.19%), Thyroid disease (9.75%), Hepatitis (2.43%), and Tuberculosis (1.21%). It is significant to note that stress is usually observed in infertile couples due to social causes (Figure 5).

### 3.7 Attitude of Infertile Couples towards Assisted Reproductive Technology (ART)

Table 4 shows the tendency of couples for assisted reproductive technology. A total of 14.16% of the subjects had a history of ART and 29.16% were interested in ART. Figure 6 shows frequency of ART procedure in N = 17 infertile couples with positive history of ART. In 70.58% couples Ovulation induction was performed followed by Intra uterine insemination (IUI) in 17.6% infertile couples and *In vitro* fertilization (IVF) in 11.76% infertile couples.

### 3.8 Family History of Infertile Couples Participated in the Study (N = 120)

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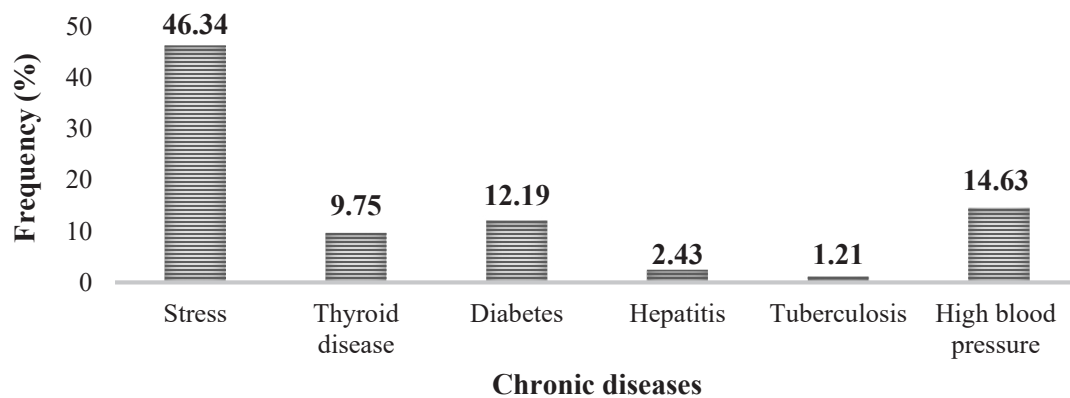


Fig. 5. Association of chronic disease in infertile subjects (N = 82).

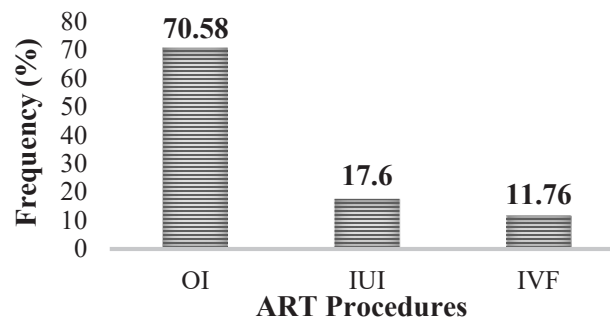


Fig. 6. History of ART procedures in infertile couples (N = 17).

show frequency of participants and horizontal lines shows familial/sporadic nature of the disease. The percentage of the sporadic infertility was 81.67% while 18.33% were having positive family history of infertility at least in one partner, familial cases (Figure 7). Among the N = 22 familial cases, 77.27% were in 'Female affected' couples while 22.72% were 'Male affected' couples. While no case with family history was found in 'Both' and 'Unexplained' categories of infertile couples. The details are shown in Figure 8.

### 3.9 Family History of Cystic Fibrosis and Hormonal Imbalance

Results about the family history of infertile females (N = 69) showed 12.5% of infertile females had a family history of cystic fibrosis and 9.16% shows hormonal imbalance (Figure 9).

## 4. DISCUSSION

Infertility is defined as the inability to conceive after attempting to do so for one year without using any contraceptive methods while having regular



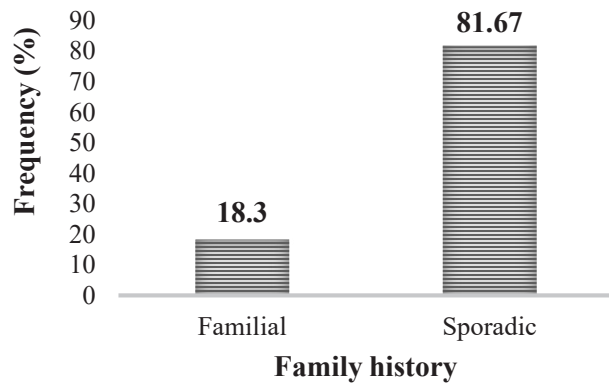


Fig. 7. Family history of infertile couples.

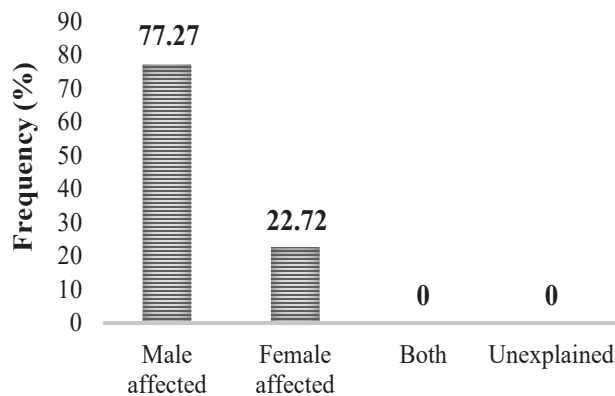


Fig. 8. Gender wise distribution of familial cases.

sexual intercourse [1]. Data analysis showed among 120 couples, 32 were with unexplained infertility. In their assessment of the literature from 1950 to 2013, Gelbaya *et al.* [12] discovered that 15% to 30% of couples would still experience infertility after having routine fertility testing performed. While 88 couples were with either single or both partners identified as infertile. In the N = 120 females, women age >35 years were 27 (22.5%). The age of the woman and her age of marriage are

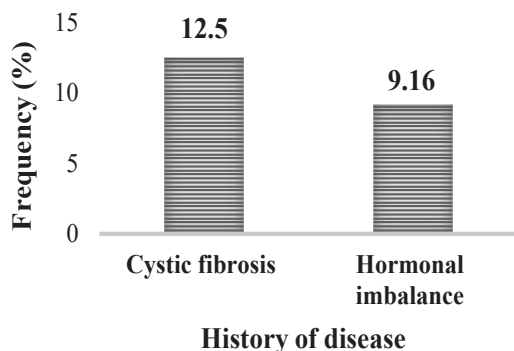


Fig. 9. Family history of CF and HI among infertile females (N = 69).

Table 4. Tendency of couples for assisted reproductive technology (ART).

S. No.	ART		N	(%)
1	History of ART (N=120)	Yes	17	14.16
		No	103	85.83
2	Interested in ART (N=103)	Yes	35	29.16
		No	85	70.83

factors that cause infertility, according to the current study and another Iranian study [4]. According to reports, one of the key factors contributing to female infertility is age [13]. The woman’s fertility peaks between the ages of 18 and 24. After that, it progressively drops until the age of 27, when it suddenly declines around the age of 35. In other words, ovarian reserves get smaller as you get older [14]. According to the current study, the majority of affected males are in the middle of their ages and have been diagnosed as infertile. An earlier study revealed that the age factor has no effect on male infertility [15].

In the present study, 21.66% of infertile women were employed and 78.33% women were unemployed. In contrast to the current study, the two studies performed in Finland, maternal occupation in the field of agriculture, and in the second case in fur farming, was found to be associated with a significantly increased risk of spontaneous abortion [16]. The findings of the present study did not show a significant correlation between female occupation and infertility. However, it is worth mentioning that most females in Pakistani population tend avoid working outside their homes. Further research with larger sample size of individuals who are directly exposed to chemicals for longer periods is recommended. In this study, 80.83% of husbands were employed and 19.16% were unemployed. Previous studies revealed that employed men’s odd ratios for male factor infertility were 1.55 times greater than those of unemployed men [17].

In the present study, infertility in overweight women 69 (57.5%) were higher compared to normal women. Another study found that the likelihood of obesity and overweight was, respectively, 4.8 and 3.8 times higher in infertile women than in fertile ones [18]. Furthermore, Cong *et al.* [19] indicated a substantial connection between the female infertility factor and BMI more than 30. In males 38 (31.66%) were over weighted. In present study,

among the 120 infertile couples, primary infertility was 47.5% versus 52.5% of secondary infertility. A similar study performed by Sami and Ali [3] in Pakistan, showed that the frequency of secondary infertility surpasses the occurrence of primary infertility. Contrarily, data from India's National Family Health Survey revealed that primary infertility is more common than secondary infertility on average [20]. The results of other research conducted in Iran were consistent with the findings of the present study, which found that the female-specific variables linked to infertility were present in (49.16%) of infertile couples. The frequency of both male and female variables, both of them, as well as other unidentified causes, was typically 20–40%, 30–35%, and 5–15%, respectively [4, 21]. In the current study the occurrence of female specific infertility was 49.16%, male infertility was observed as 15.83%, in 8.33% infertile couples, both partners were affected, and 26.66% of the 120 couples had unexplained infertility. Result analysis manifested majority of the infertile couples were with multiple causative factors where just few couples were observed with a single cause of infertility. A comparable study carried out in Iran revealed that most infertile couples gave more than one explanation for their infertility, with only a small minority giving only one [4].

According to the findings of the current study, erection problems accounted for 48.27% of all 29 male infertiles, making them the most common cause of male infertility. The most often identified reasons, as determined by the results of the semen analysis, were azoospermia (17.24%) and oligospermia (10.34%). According to a prior Chinese study, varicocele is the most common cause of male infertility [22]. The high incidence of erectile dysfunction causing infertility can be attributed to the high frequency of males in older age groups, as the severity and occurrence of erectile dysfunction tend to increase consistently with age in males. In the present study it has been noted that hormonal imbalance had a significant role in ovulation disorders. Hormonal imbalances lower the quantity of eggs in the ovary and even lower the quality of the egg cell. Low gonadotropin levels cause infertility in 5–10% of women, while decreased hypothalamic GnRH secretion causes secondary estradiol. According to one study, tubal factors and ovarian causes were the two most common reasons of female infertility [23].

Several studies from Pakistan have identified several genetic factors responsible for infertility in consanguine. For instance, frameshift mutation in KCTD19 and SPATA22 has been reported to be associated with infertility in Pakistan [8, 24]. Additionally, MTHFR gene plays a major role in regulation of spermatogenesis with its C667T allele variants can disturb the process ensuing male infertility. However, a study by Fatima *et al.* [25] reported that MTHFR C677T polymorphism is not significantly associated with increased risk of male infertility in Pakistan. The present study showed that the underlying chronic disease may influence fertility. Glazer *et al.* [26] observed that infertile males had lower testosterone levels and higher levels of anxiety and stress. This increased the production of stress hormones and increased the risk of cardiovascular disease, diabetes, and death. The results of the current study indicated a connection between drug addiction and male infertility. According to another study, 60% of smokers were infertile [14]. Smoking alters a number of sperm characteristics, including quantity, motility, and antioxidant properties. This has an impact on the sperm normal morphology. In studies conducted by Penzias *et al.* [27] and Caserta *et al.* [28], it was found that cigarette smoking had a significant correlation with oligospermia (low sperm count) in men, as well as with progressive motility and reduced sperm volume. However, these studies did not find a significant association between cigarette smoking and alterations in sperm morphology.

## 5. CONCLUSIONS

In conclusion, our study identified the primary causes of infertility, with a higher prevalence observed in female-related cases. The most common causes of female infertility were menstrual disorders, hormonal imbalances, Polycystic Ovary Syndrome (PCOS), and endometriosis. These conditions, which disrupt the normal reproductive processes, were found to significantly contribute to the high rate of infertility among women. On the other hand, male-related infertility was predominantly caused by oligospermia (low sperm count), azoospermia (absence of sperm), and erectile dysfunction. These conditions, which affect sperm production and delivery, were the leading factors contributing to male infertility.

## 6. ETHICAL STATEMENT

The Undergraduate Research Ethical Committee, Department of Zoology, Kohat University of Science and Technology (KUST), Kohat, granted approval for the current study wide Ref. No. ZO-220192049, dated: August 17, 2021.

## 7. CONFLICT OF INTEREST

The authors declared no conflicts of interest.

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