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Original Article

Induced Perceived Infertility Related to Psychological Distress among Adult Women Receiving Chemotherapy at a Tertiary Care Hospital, Karachi, Pakistan; an Analytical Cross-Sectional Study

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Abstract

Globally, many individuals of reproductive age are affected by cancer and may experience perceived infertility because of its treatment. The primary objectives of this study were to estimate the mean score of fertility-related distress and to examine the association between perceived infertility and distress among adult women receiving chemotherapy at a tertiary care hospital in Karachi, Pakistan. The secondary objective was to assess the relationship between fertility-related distress and other associated factors in this population.

This was an analytical cross-sectional study conducted at a single private tertiary care teaching hospital in Karachi, Pakistan. A sample size of 137 participants was calculated; however, 150 participants successfully completed the survey. The inclusion criteria comprised female patients aged 18 to 50 years undergoing chemotherapy, with no pre-existing infertility issues. Exclusion criteria included a prior psychiatric diagnosis, history of surgery involving reproductive organs, reproductive organ cancer, pregnancy, and single/unmarried status.

Fertility-related distress was assessed using the Fertility Problem Inventory Scale, while associated factors were evaluated through a structured questionnaire. The participants had a mean age of 39.75 ± 6.85 years and demonstrated a mean fertility-related distress score of 79.30 ± 1.30. Multivariable linear regression analysis revealed that women who were not planning to have children (β = 6.43, 95% CI: 2.21–10.64) and those undergoing radiation therapy (β = 20.86, 95% CI: 15.77–25.94) were significantly associated with higher distress levels. Perceived infertility was not directly associated with distress. However, a significant interaction was observed between perceived infertility and family status, resulting in a negative effect (β = −2.5, 95% CI: −4.7 to −0.2).

Healthcare providers should proactively address fertility-related concerns and provide timely support to women undergoing cancer treatment. Such interventions may help reduce distress and improve the overall psychological well-being of patients.

Keywords: Fertility-Related distress; Perceived infertility; Adult women with cancer; Chemotherapy

1. Introduction

Worldwide, millions of individuals of childbearing age are affected by cancer and experience perceived infertility because of cancer treatment [1]. Among these individuals, many women frequently perceive infertility as a stressful stimulus that may contribute to psychological distress later in life [2]. Similarly, for women diagnosed with cancer during the early stages of life, the disease not only affects their physical health but also threatens their future ability to have children, which can adversely impact their quality of life (QOL) [3, 4]. Perceived infertility has been defined as an individual's personal belief regarding their inability to conceive due to chemotherapy, irrespective of medical evaluation, and is based more on subjective understanding than on objective medical assessment [5]. Consequently, perceived infertility can result in considerable distress, as it interferes

with the achievement of important personal and family-related life goals.

Cancer treatment can significantly impair fertility among patients, affecting not only young adults but also children and adolescents [6]. According to the World Health Organization (WHO, 2020), approximately 18.1 million new cancer cases and 9.6 million cancer-related deaths were reported globally in 2018, and these figures are projected to double by the year 2040 [7]. Furthermore, infertility among cancer patients has been reported to range between 30% and 75% [8]. A study conducted in Sweden reported that the likelihood of having children and becoming parents among cancer patients was reduced by nearly 50% compared to their siblings who did not have cancer [9]. The "American Society of Clinical Oncology Clinical Practice Guideline (ASCOPO) 2013" recommends comprehensive discussions regarding fertility-related concerns and available options, particularly for cancer patients in their reproductive years. The guideline further emphasizes the importance of involving spouses or family members to facilitate preparation and exploration of fertility preservation strategies during the initial phase of treatment [10].

According to the Karachi Cancer Registry Database (KCRD), female cancer cases accounted for 52.5% and male cancer cases for 47.5% of the total cancer burden recorded up to 2019 [11]. In addition, Pakistan reported approximately 19 million cancer cases in the year 2020 [9, 11]. A study conducted in South India examining the long-term effects of childhood cancer revealed that 24% of childhood cancer survivors were diagnosed with infertility during adulthood [12]. Emerging evidence regarding chemotherapy-related perceived infertility suggests a substantial risk of long-term infertility-related psychological distress influenced by multiple contributing factors. An Iranian study reported that the prevalence of infertility-related distress ranged from 25% to 60% [13]. Therefore, infertility is considered a major source of distress as societal norms often associate it with failure on physical, emotional, psychological, sexual, cultural, and social dimensions. Although fertility-related concerns are experienced by both men and women, women often carry a greater burden because of societal expectations and family pressures related to childbearing [14].

Female cancer patients are widely recognized as one of the most vulnerable populations for experiencing perceived infertility due to intensive chemotherapy treatment [1, 15]. Compared to males, female cancer patients are more likely to experience perceived infertility because of societal and familial expectations regarding conception and the stigma associated with being unable to bear children [16]. Moreover, many patients remain unaware of the long-term severity and consequences of infertility caused by chemotherapy, which may subsequently contribute to psychological distress later in life [17]. In Pakistan, there remains a significant gap in understanding fertility-related psychological distress among female cancer patients. Therefore, this study aims to calculate the mean score of fertility-related psychological distress, assess the correlation between perceived infertility and fertility-related psychological distress, and identify the factors associated with fertility-related psychological distress among adult women undergoing chemotherapy at a tertiary care hospital in Karachi, Pakistan.

2. Materials and Methods

2.1. Study Design and Setting

An analytical cross-sectional study was conducted from May 2023 to July 2023, at Aga Khan University Hospital, Karachi, Pakistan. The study design was employed to investigate the association between perceived infertility and fertility-related psychological distress among cancer patients. Data collection was carried out with patients who were physically present during their chemotherapy sessions at the hospital, in the presence of trained healthcare professionals. In addition, the hospital's well-established electronic medical record system and comprehensive cancer registry was utilized for gaining access to local cancer epidemiology database.

2.2. Participants and procedures

A non-probability purposive sampling technique was employed to recruit participants. Female adult patients visiting the oncology department, including outpatient clinics, daycare settings, and inpatient wards, were approached to assess their eligibility based on predefined inclusion criteria. Only females aged between 18-50 years of age, who were undergoing chemotherapy, without any pre-existing infertility-related conditions and able to contribute to answering the research questions, were considered eligible for enrollment. Any female patient with prior diagnosis of any mental disorder, those with a history of reproductive organ surgery or reproductive organ cancer, pregnant women, and women who were single or unmarried were excluded from the study. Patients who fulfilled all eligibility requirements were consented accordingly. **Figure** 1 illustrates the participant recruitment process for the study.

2.3. Sample Size

Several international studies have reported a correlation between perceived infertility and fertility-related psychological distress [3]. Based on the available literature, the maximum sample size was estimated using a correlation coefficient of -0.25 while considering the null hypothesis correlation as zero. A minimum sample size of 124 patients was required to achieve 80% statistical power using a two-sided test with a significance level of 0.05. To compensate for potential refusals and non-response,

the sample size was further inflated by 10%. Consequently, the final calculated sample size was 137 cancer patients. However, to further enhance the statistical power of the study, a total of 150 participants were ultimately recruited, evaluated, and included in the analysis. The sample size calculation was performed using statistical software, STATA version 15.0.

Figure 1: Flowchart of Participants

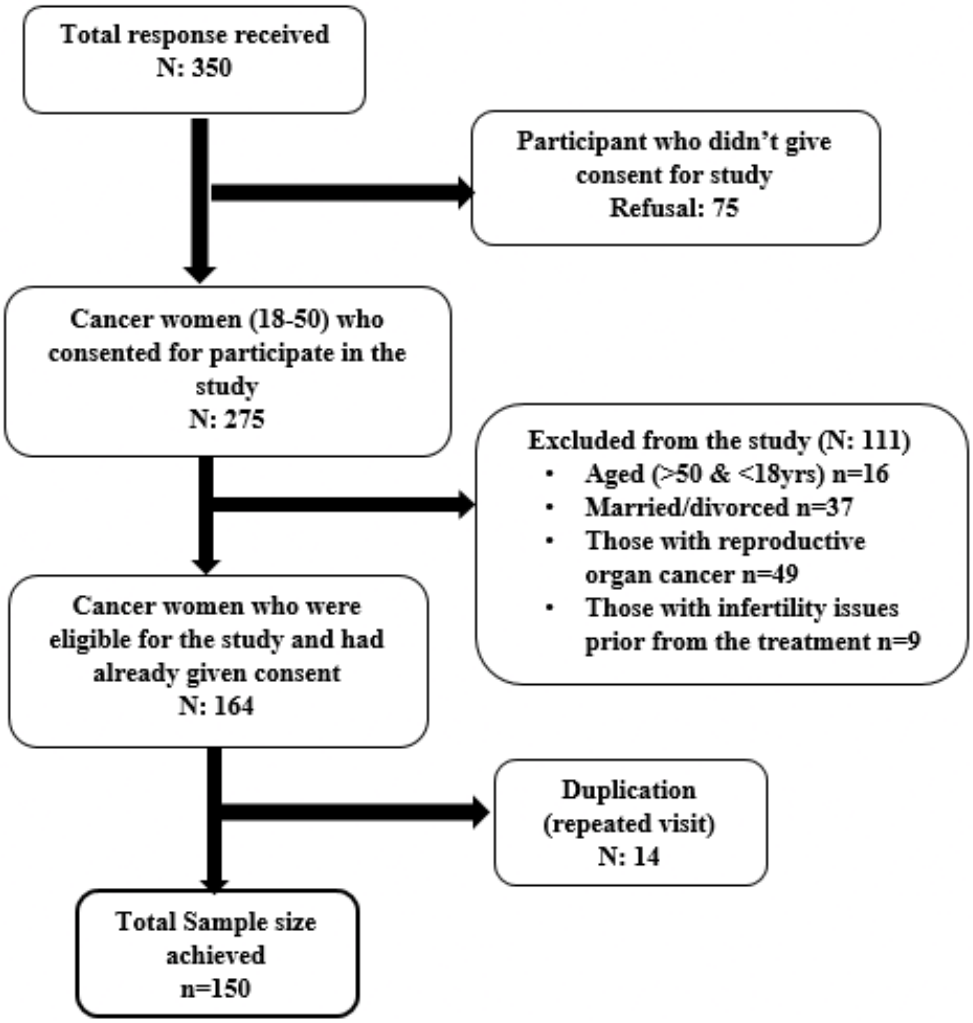

Figure 1: Flowchart showing the process of participant recruitment

2.4. Data Collection

Data collection was initiated using a screening questionnaire through which all eligible participants were identified. Participants who met the eligibility criteria then proceeded to the structured questionnaire for further data collection.

2.4.1 Fertility related psychological distress outcome by Fertility Problem Inventory Tool

Fertility-related psychological distress among women with cancer was assessed using the Fertility Problem Inventory (FPI) tool. This instrument comprises five major domains:

- Rejection of Childfree Lifestyle
- Need for Parenthood
- Social Concern
- Sexual Concern
- Relationship Concern

A shortened 27-item version of the scale was utilized in this study. The tool was based on a 6-point Likert scale ranging from 1 ("Strongly Disagree") to 6 ("Strongly Agree"). The total score of the instrument ranged from 27 to 162. The individual domain scores were combined to generate a global stress score, where higher scores indicated greater levels of fertility-related psychological distress among women with cancer.

Content validation of the Fertility Problem Inventory tool was conducted for this study. Although the scale has been internationally validated, it was considered necessary to validate it within the Pakistani context to ensure its cultural relevance, clarity, and appropriateness for the study population. The Cronbach's alpha for both relevancy and clarity were found to be 0.96, indicating excellent internal consistency and reliability of the tool.

2.4.2 Primary exposure-Perceived infertility by Infertility Knowledge Questionnaire Scale

Perceived infertility scores were assessed using the Infertility Knowledge Questionnaire Scale (IKQS). This scale consists of 11 items that are categorized into two domains: general infertility knowledge, comprising two items, and cancer- or treatment-specific infertility knowledge, consisting of nine items. Each participant was asked to respond to the questionnaire items using one of three response options: "true," "false," or "don't know." The total score of the scale ranges from 0 to 11, with each correct response contributing one point toward the overall score. Lower scores on the IKQS indicate a lower level of infertility-related knowledge and a higher degree of perceived infertility among the participants.

2.4.3 Social Demographic Characteristics and Cancer-Related Characteristics

This study also examined various sociodemographic and cancer-related characteristics. Furthermore, body weight and height measurements of the participants were obtained from hospital records, and body mass index (BMI) was subsequently calculated using these measurements. All participant characteristics are shown in **Table** 1.

2.5. Statistical Analysis

All statistical analyses were performed using STATA software (version 15.0). Frequencies and percentages were reported for sociodemographic, nominal, and categorical variables. In addition, measures of central tendency were calculated for quantitative variables.

To evaluate the relationship between fertility-related psychological distress and perceived infertility among adult women with cancer, correlation coefficients were computed. Furthermore, univariate and multivariable linear regression analyses were performed to examine fertility-related psychological distress in relation to different risk factors. Crude and adjusted beta coefficients, along with their corresponding 95% confidence intervals, were reported. A p-value of less than 0.05 was considered statistically significant. Additionally, all plausible overall interactions were assessed, and the cutoff value for interaction was set at <0.1. Model assumptions, including linearity, normality of residuals, homoscedasticity, and multicollinearity, were also evaluated to ensure the validity of the regression analyses.

3. Results

3.1. Baseline Characteristics of Participants

The baseline characteristics of the participants are presented in **Table** 1. A total of 150 female cancer patients, representing various tumor types, participated in the study. The mean age of the participants was 39.753 ± 6.850 years. Approximately 49% of the participants were living in a joint family system. Regarding educational attainment, 37.3% had completed higher education. Furthermore, 25.3% of the women had no children and 44.67% reported that they did not desire to have children. 56% had no prior history of infertility issues.

Among the reported cancer types, 69.3% of women had breast cancer, and 54% were diagnosed at stage II cancer. The median number of chemotherapy cycles among the surveyed women was 8 ± 11.00 and 72.6% of participants received radiation therapy as part of their treatment regimen.

Table 1: Baseline characteristics of participants

Variables	Frequency (percentage) *Mean (Standard Deviation) N=150
Age* (in years)	39.75 (6.85)
Ethnicity	
Balochi	17 (11)
Chitrali	07 (05)
Gujarati	25 (17)
Sindhi	27 (18)
Urdu speaking	56 (37)
Hindu	06 (04)
Punjabi	06 (04)
Other	06 (04)
Education level	
Less Than Matric	30 (20)
Matric	24 (16)
Intermediate	40 (27)
Higher Degree	56 (37)
Employment status	
Unemployed	17 (11)
Homemaker	99 (66)
Employed	34 (23)
Childbearing status	
No child	38 (25)
1 child	40 (27)
2 children	31 (21)
3 and more children	41 (27)
Planning for children	
Yes	83 (55)
No	67 (45)
Smoking	
No	129 (86)
Yes	21 (14)
Drinking	
No	137 (91)
Yes	13 (09)
Family history of infertility	
No	84 (56)
Yes	66 (44)
Family status	
Nuclear family	76 (51)
Joint family	74 (49)
Co-morbidity	
No	66 (44)
Yes	84 (56)
BMI	
Underweight	11 (07)
Normal weight	44 (29)
Overweight	45 (30)
Obese	50 (34)
Household members*	12.86 (5.60)
Earning members*	3.39 (1.74)
Total earnings per month (PKR)	
5,000-25000	54 (36)

25000-50,000	14 (09)
50,000-75,000	07 (04)
75,000-100,000	34 (23)
100,000 and above	41 (27)
Cancer Related Characteristics	
Cancer site	
Breast and lung	104 (69)
Head and neck	09 (06)
Abdominal	18 (12)
Musculoskeletal	05 (03)
Others	14 (09)
Cancer stage	
Stage 1	13 (09)
Stage 2	81 (54)
Stage 3	56 (37)
Chemotherapy cycles*	08 (11.00)
Highest dose* (mg/m^2)	1169.01 (1575.68)
Radiation	
No	41 (27)
Yes	(73)

Asterisk (*): Mean (Standard Deviation); (Mg/m^2): milligrams per square meter

3.2. Mean Scores of Perceived Infertility and Fertility Related Psychological Distress

As measured by the Fertility Problem Inventory Scale (FPI), the average level of fertility-related psychological distress and experiencing fertility-related issues was 79.30 ± 1.30. In addition, perceived infertility, as assessed using the Infertility Knowledge Questionnaire Scale (IKQS), showed a mean score of 3.88 ± 1.87. The study demonstrated a negative association between perceived infertility and fertility-related psychological distress, with a Pearson correlation coefficient of -0.04 **(Figure** 2**)**.

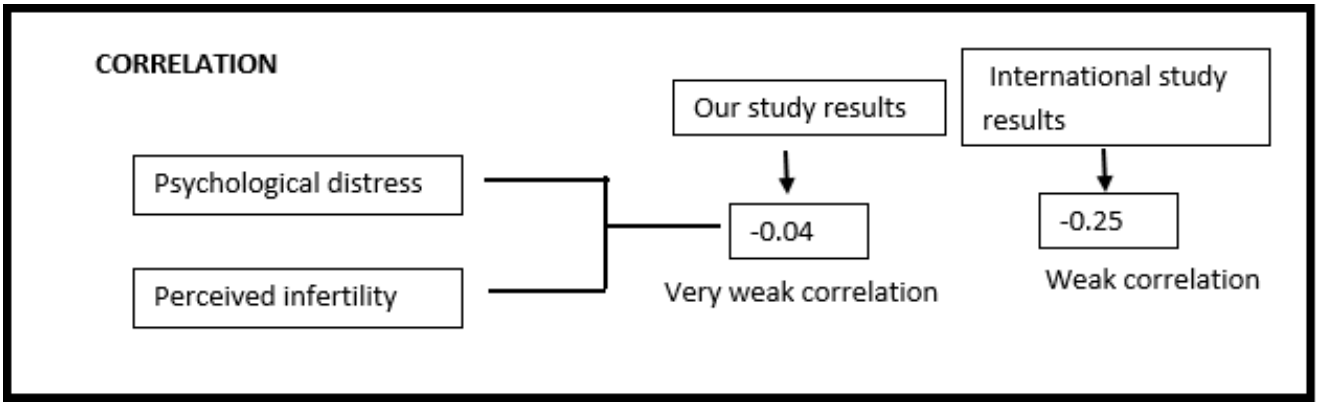

Figure 2: Correlation between fertility-related psychological distress and perceived infertility

3.3. Fertility related psychological distress and its predictors

Predictors of fertility-related psychological distress are presented in **Table** 2. The findings indicate that the estimated mean score of fertility-related psychological distress increases by 20.86 (95% CI: 15.89, 25.82) among women with cancer who received radiation therapy compared to those who did not receive radiation. In addition, the estimated mean score of fertility-related psychological distress increases by 6.43 (95% CI: 2.49, 10.37) among women who are currently not planning for a child compared to those who are planning for a child.

An interaction between perceived infertility and family status **(Figure** 3**)** was identified, with a p-value of 0.028, indicating a statistically significant interaction between these two variables. Specifically, for each one-unit increase in the perceived infertility score among women living in a joint family, the mean fertility-related psychological distress score was estimated to decrease by 2.5 units compared to women living in a nuclear family. Robust regression analysis was conducted to

appropriately account for potential outliers and influential observations within the dataset. Overall, 39.3% of the variability in mean psychological distress among female cancer patients was explained by radiation exposure, childbearing plans, and the interaction between perceived infertility and family status.

Table 2: Linear Regression Analysis of Factors Associated with Fertility-Related Psychological Distress

Characteristics	**Crude β (95% CI)**	**Adjusted β (95% CI)**
Perceived Infertility Score	-0.39 (-1.78 – 0.98)	–
Radiation		
No	1	1
Yes	17.77 (12.72 – 22.82)	20.86 (15.89, 25.82)
Planning for children		
Yes	1	1
No	9.21 (4.21 – 14.21)	6.43 (2.49, 10.37)
Family status		
Nuclear family	1	–
Joint family	2.52 (-2.64 – 7.69)	
Interaction between Perceived Infertility Score and Family Status		
Perceived infertility with nuclear families	–	0.70 (-0.70, 2.12)
Perceived infertility with joint family		-2.50 (-5.12, -0.27)
Zero perceived infertility with joint family		18.76 (7.95, 29.57)
Zero perceived infertility with nuclear family		Reference
F_{cal}**: 18.68 P-value: <0.001 R-square: 0.3934**		

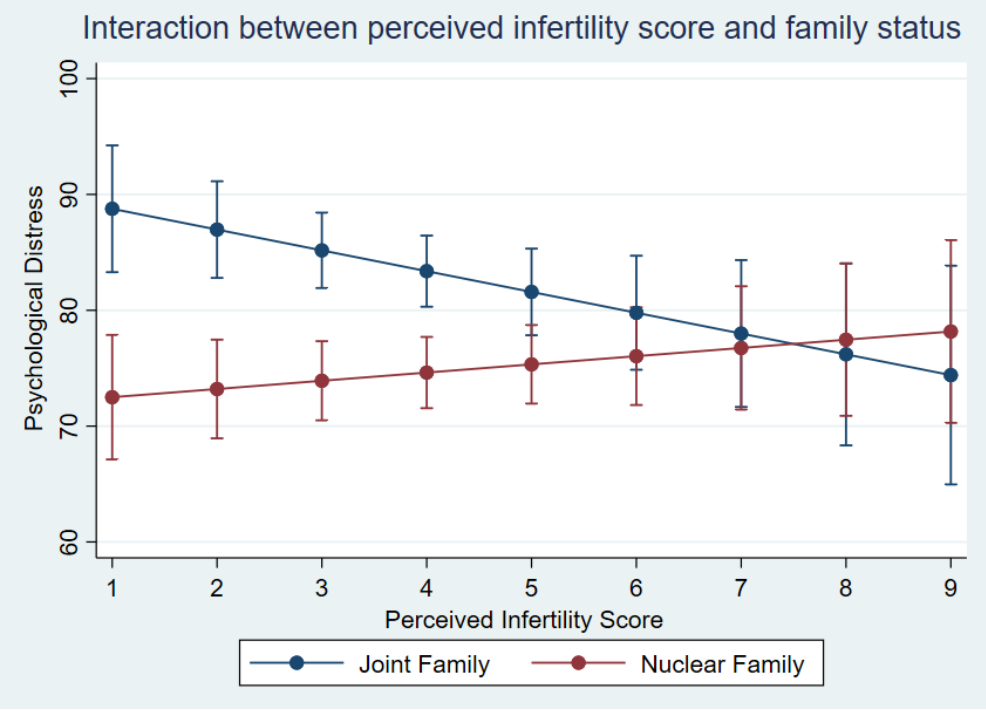

Figure 3: Interaction Plot Showing the Association of Perceived Infertility Score and Family Status with Psychological Stress

4. Discussion

The present study estimated the mean score of fertility-related psychological distress and examines the association between perceived infertility and psychological distress among adult females receiving chemotherapy. Furthermore, this study also assessed the association between psychological distress and other related factors in these women.

The study findings indicated that the mean score of fertility-related psychological distress among women was at a moderate level. This level of distress was notably higher when compared to developed countries, where the mean distress score has

been reported to be low [18]. A study conducted in Australia provided important insights into the subjective experiences of women undergoing infertility-related distress. The study identified multiple negative emotional themes expressed by women, including feelings of horror, grief, absence, heartbreak, and intense emotional pain. These themes reflected the depth of distress experienced in relation to infertility concerns [19, 20].

One of the significant factors contributing to distress among female cancer patients is inadequate knowledge regarding infertility caused by chemotherapy, along with cultural stigma [21–23]. Our study supported this finding by demonstrating that the mean score for fertility-related knowledge was remarkably low. However, it is important to note that this study did not find a statistically significant association between perceived infertility and fertility-related psychological distress. This lack of significance may be attributed to the relatively small sample size. These findings appear to contrast with previous literature, as a study conducted in Taiwan reported a highly significant negative impact of perceived infertility on the lives of cancer patients, particularly among women, with this impact being strongly associated with psychological distress [24].

The lack of desire to have children at a given time has been associated with insufficient access to fertility-related information and counseling, which limits opportunities for receiving appropriate guidance and may contribute to distress later in life [23, 25]. Our study also identified a statistically significant association between women who were not currently planning to have children and psychological distress. These findings are consistent with a study conducted by Gabriela M. A. *et al.,* which reported that women who desired children and were actively engaged in family planning were more likely to ask questions and seek clarification. In contrast, women who did not initially wish to have children at the start of treatment were more likely to have limited knowledge regarding fertility issues, which could subsequently lead to distress [4]. This highlights the importance of a more inclusive and proactive approach to providing fertility-related education and support to all individuals undergoing cancer treatment [26].

Our results also demonstrated that women who received radiation therapy experienced a greater impact on perceived infertility. This suggests that radiation treatment may have a more pronounced effect on fertility concerns among female cancer patients [27]. This observation may be influenced by cultural stigma surrounding radiation therapy, which is often perceived as affecting not only the targeted cancer site but also the entire body, including reproductive organs [28]. Such beliefs and perceptions may contribute to heightened concerns regarding infertility among women undergoing radiation treatment [29]. The American Cancer Association (2020) highlighted, the effect on fertility in female patients during brain cancer treatment by indicating that radiation may inadvertently impact the pituitary gland, thereby disrupting hormonal signals responsible for ovulation. The extent of this effect depends on several factors, including the dose and duration of radiation therapy, highlighting the complex relationship between radiation treatment and fertility [30]. This finding indicates that irrespective of the cancer type or treatment regimen, female cancer patients may be vulnerable to fertility-related issues that need to be addressed through counselling [31].

Existing literature also provides evidence that the joint family system can be a significant contributor to cultural and social pressures, potentially affecting mental well-being [32]. In many developing countries, including Pakistan, joint family systems often involve living with extended family members, which introduces complex social and cultural dynamics that may influence psychological health [33]. Furthermore, strong societal pressure, particularly from in-laws, to have children is commonly reported in many developing settings [34]. Such social and familial expectations can place a substantial psychological burden on women, especially those facing health challenges such as cancer or cancer-related infertility, contributing to stress, anxiety, and distress [35]. In our study, the association between living in a joint family system and perceived infertility was significantly linked to psychological distress. Given the strong relationship between these predictors, it is evident that these factors have a substantial combined effect on an individual's distress level. This highlights the interconnected nature of family structure and perceived infertility and their collective impact on psychological well-being. Understanding these interactions is essential for developing comprehensive support and intervention strategies to address the unique needs of women experiencing cancer-related fertility concerns.

Our study results indicate that healthcare providers should routinely assess and monitor distress levels in cancer patients and provide a comprehensive understanding of their condition to reduce long-term psychological stress. One way is to effectively refer patients to counseling services. In addition, discussions regarding fertility preservation options should be initiated prior to starting systemic oncological treatment to reduce distress in such patients. An important aspect of these recommendations is that healthcare providers, including nurses and physicians, should also receive appropriate training, every few months, to effectively address the psychological aspects of cancer care. The role of healthcare providers is extremely important as it helps to reduce the stigma associated with infertility, especially in a patient living in a joint family system. In lieu of this, public awareness programs could serve as essential tools to improve knowledge and understanding of fertility issues during cancer treatments.

5. Limitation and future perspectives

Despite providing valuable insights, this study has certain limitations. As an analytical cross-sectional design was used, it does not allow for the establishment of a temporal relationship between perceived infertility and fertility-related psychological distress. The exclusive focus on female cancer patients also limits the generalizability of the findings to male patients. In

addition, being a single-center study further restricts the generalizability of the results; therefore, multicenter studies are recommended to obtain more robust and widely applicable evidence. Moreover, the subjective and culturally sensitive nature of these issues may have introduced potential response and non-response bias. The relatively small sample size may also have limited the ability to identify a broader range of factors associated with fertility-related psychological distress.

Larger longitudinal studies and controlled trials addressing these limitations are recommended to further establish and confirm the relationship between perceived infertility and fertility-related psychological distress. Such studies may provide deeper insights into effective interventions to reduce distress among cancer patients facing fertility-related concerns.

6. Conclusion

The findings of this study underscore the critical importance of providing comprehensive information regarding infertility-related issues. Moreover, healthcare providers should take a proactive role in recognizing and addressing these concerns in a timely manner among all women diagnosed with or undergoing treatment for any type of cancer, to reduce psychological distress throughout the treatment process. Furthermore, additional counseling sessions that involve family members may be beneficial in alleviating family-related pressures while societal awareness programs to disseminate knowledge about fertility issues resulting from cancer treatments may help to reduce persistent judgment and stigma.

7. Declarations

Funding

This research received no funding.

Author Contributions

MH conceived and designed the study, performed data collection and analysis, interpreted the data and results, and drafted the initial manuscript. YR, FB, TA: reviewed, guided and provided overall supervision throughout the study. The final version of the manuscript has been read and approved by all authors.

Ethics Approval and Consent to Participate

Ethical considerations aligned with the Declaration of Helsinki 2022 were adhered to in this study. Approval for the study was obtained from the Aga Khan University Ethical Review Committee, with the reference number 2023-8523-26995.

Data Availability Statement

The datasets used and/or analyzed during this study are available upon reasonable request from the corresponding author.

Conflicts of Interest

The authors declare no conflicts of interest.

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Use of Artificial Intelligence

During the preparation of the manuscript, authors used ChatGPT for language editing, clarity, and preparation of graphics. After using the tool, authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

8. Abbreviations

The following abbreviations are used in this manuscript:

FPI	Fertility Problem Inventory
IKQS	Infertility Knowledge Questionnaire Scale
PKR	Pakistani Rupee
QOL	Quality of Life
WHO	World Health Organization
ASCO	American Society of Clinical Oncology
KCRD	Karachi Cancer Registry Database
BMI	Body Mass Index
SD	Standard Deviation
CI	Confidence Interval

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