ANXIETY AND DEPRESSION AMONG PATIENTS TREATED AT TWO FERTILITY CENTRES IN NAIROBI; PREVALENCE AND ASSOCIATED FACTORS: A DESCRIPTIVE CROSS-SECTIONAL STUDY WITH A SUB-GROUP ANALYSIS

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DECLARATION

This dissertation is my original work and has not been presented for a degree in any other University.

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DEDICATION

This dissertation is dedicated to all couples afflicted with infertility. May you be filled with hope and experience peace as you pursue treatment.

He gives childless couples a family, gives them joy as the parents of children. Halleluyah!

~Psalm 113:9 (The Message version)

DEFINITION OF OPERATIONAL TERMS

Anxiety: Defined as an emotion characterized by feelings of tension, worried thoughts and physical changes like increased blood pressure.

Depression: Defined as a mood or emotional state that is marked by feelings of low self-worth or guilt and a reduced ability to enjoy life.

Infertility: Defined as the failure to achieve a pregnancy within 12 months of unprotected intercourse or therapeutic donor insemination in women younger than 35 years or within 6 months in women older than 35 years.

Primary infertility: Refers to those who have never conceived.

Secondary infertility: Refers to those who have had a previous pregnancy but subsequently fail to conceive.

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LIST OF ABBREVIATIONS AND ACRONYMS

ART	Artificial Reproductive Technology
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
COPD	Chronic Obstructive Pulmonary Disease
DASS	Depression Anxiety Stress Scales
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders- IV
EPDS	Edinburgh Postnatal Depression Scale
ERC	Ethics and Research Committee
FPI	Fertility Problem Inventory
HADS	Hospital Anxiety Depression Scale
ICPD	International Conference on Population and Development
IUI	Intrauterine Insemination
IVF	In Vitro Fertilization
KNH	Kenyatta National Hospital
MHI-5	Mental Health Inventory-5
MINI	Mini International Neuropsychiatry Interview
PESA	Percutaneous Epididymal Sperm Aspiration
PGD	Preimplantation Genetic Diagnosis
PGS	Preimplantation Genetic Screening
SCID-I	Structured Clinical Interview for DSM-IV
SDS	Self-rating Depression Scale
SF-36	Short-form Health Survey
SRHR	Sexual and Reproductive Health Rights
STAI	State Trait Anxiety Inventory
TESA	Testicular Sperm Aspiration
UoN	University of Nairobi
WHO	World Health Organization

ABSTRACT

Background: WHO recognizes infertility as the 5th highest cause of disability under the age of 60 globally. Studies have shown a link between infertility and psychiatric problems, whereby earlier studies blame infertility on psychiatric problems, and recent studies point to psychiatric problems as a sequel of infertility. There is a preponderance of generalized anxiety disorder and depression among infertile individuals. These conditions reduce the chances of achieving a pregnancy and affect continuity of care. Addressing psychological concerns in the management of infertility can improve follow-up and outcomes of the affected patients.

Objective: To establish the prevalence of generalized anxiety disorder and depression along with their associated factors among patients undergoing treatment for infertility at two fertility centres in Nairobi.

Methodology: Using a cross-sectional study with a sub-group analysis design, 124 patients attending two fertility centres between January and March 2022 were recruited into the study. Questionnaires incorporating the Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI) were administered for self-reporting of depressive and anxiety, respectively.

Data analysis: Data was analyzed using Statistical Package for Social Science (SPSS) version 26.0. Frequencies and percentages were used to present categorical data while means with standard deviations were used to present continuous data. Sociodemographic and reproductive characteristics were subjected to Pearson's Chi-square tests, thereafter bivariate and multivariate logistic regression analysis was used to determine the factors associated with generalized anxiety disorder and depression. A p-value of <0.05 was considered to be statistically significant.

Results: A total of 124 questionnaires were analysed in the study. The mean age of the study participants was 37 ± 6.212 years. A majority of the participants were female (83%), Christians (94%), married (94%), employed (68%), urban dwellers (73%) and obese (36%). Most of them had not been married before (59%) and most had tertiary education (90%). A minority of them were smokers (2%) and alcohol consumers (20%). The average length of marriage was 8.04 ± 5.11 years. Primary infertility was the most common type of infertility (56%). The mean duration of infertility was 6.12 ± 4.342 years. Female factor was the predominant cause of infertility (40%). Most of the participants were ART naive (63%). ART was the most common treatment modality (55%). Majority of the patients did not have a concomitant illness in the reproductive tract (90%). The prevalence of generalized anxiety disorder was found to be 50% and that of depression was found to be 19%. Factors associated with generalized anxiety

disorder were duration of infertility (p=0.03, AOR 1.20, 95%CI 1.02,1.42), previous marriage (p=0.017, AOR 3.02, 95%CI 1.22,7.46), lack of tertiary education (p=6.39, 95%CI 1.38,29.56),and co-existing depression (p=0.003, AOR 8.35, 95%CI 2.09,33.25). Factors associated with depression were duration of infertility (p=0.047, AOR 1.13, 95%CI 1.00,1.28), concomitant illnesses in the reproductive tract p=0.018, AOR 6.12, 95%CI 1.37,27.37) and co-existing generalized anxiety disorder.

Conclusion: Depression and generalized anxiety disorder affect patients undergoing treatment for infertility in our setting. Psychological support should be incorporated into the routine management for infertility.

CHAPTER ONE: INTRODUCTION

1.1. Background to the study

Infertility refers to the inability to conceive within 12 months of frequent and unprotected coitus. For women above the age of 35 years, the cut-off is 6 months (1). Involuntary childlessness affects 15% of partners within the child-bearing age globally (2). WHO estimates that 1 in 4 couples in low- and middle-income countries are affected by infertility.

Involuntary childlessness is categorized into two: primary and secondary. Primary infertility denotes the inability to conceive among couples without a prior history of conception while secondary infertility refers to the inability to conceive in the setting of a prior history of conception.

The causes of infertility can be ascribed to the woman, man, both partners, or unknown factors. Female factor accounts for a third of the cases, male factor accounts for another third, while another third is due to a consolidation of the two. About 10% of cases are idiopathic (3).

Approximately 30-40% of female factor infertility results from problems related to ovulation, and includes: anovulation/oligo-ovulation, decreased ovarian reserve, and a deficient secretory phase of the menstrual cycle. Other causes of female infertility include pelvic endometriosis as well as diseases affecting the fallopian tubes, uterus, and cervix. (4).

Male factor infertility can be related to extra-gonadal factors, factors affecting the testes, and factors related to obstruction of ducts within the genital tract (4). Pretesticular factors include psychosexual factors, drugs, genetic disorders, and hormonal factors. Testicular factors include Sertoli cell only syndrome and abnormal spermatogenesis secondary to drugs, varicoceles, or infections. Post-testicular causes include congenital or acquired obstruction of the efferent duct. Most cases of male infertility are idiopathic.

A decline in fertility has been noted in Kenya as well as other African countries (5). Over the last three decades, there has been an annual increase in the prevalence rate of infertility by 0.370% for women and 0.291% for men, respectively (6). A systematic review of sperm count trends by Levine et al. showed a significant decline between 1973 to 2011(7).

WHO recognizes infertility as the 5th highest cause of disability under the age of 60 globally (8). In addition to this, WHO recognizes it as a global public health issue because it affects several aspects of one's being, including identity, self-esteem, relationships, and future plans. In 2017, the global prevalence of mental health disorders was 10.7% (9). In Kenya, common mental disorders account for 10.8% of the disease burden in the country (10). The most common mental health problems in Kenya are mood and anxiety disorders with a 26.3% prevalence of depression and 9.3% prevalence of generalized anxiety disorder in the general population (11).

Infertility was initially thought to result from psychiatric disorders but psychologists now admit that psychiatric disorders can be a consequence of infertility (12). The Kübler-Ross model of grief has been widely used by psychologists to describe how people respond to the experience of infertility (13). Furthermore, the experience is likened to dealing with severe clinical illnesses or the anguish of dealing with the loss of a partner (14). Among the mental health problems resulting from infertility are depression, anxiety disorders, personality disorders, somatization, sexual dysfunction, addiction problems, and eating disorders (15).

Among the different psychiatric conditions, there is a preponderance of generalized anxiety disorder and depression among patients with infertility (16). A diagnosis of depression is made if a minimum of five of the following symptoms are noted within a period of two weeks, affecting the quality of life of the affected person: depressed mood, insomnia/hypersomnia, anhedonia, loss of energy, indecisiveness or lack of concentration, a change in weight or increased/decreased appetite, feelings of worthlessness, psychomotor agitation/retardation, and preoccupation with thoughts of death or suicidal ideation (17). On the other hand, generalized anxiety disorder is characterized by uncontrolled anxiety or worry on a majority of days within six months, and inability to control the worry. Features of anxiety include easy fatiguability, impatience, inattention, agitation and muscle strains. The anxiety, in this case, should not be attributable to any substance and should be severe enough to impair one's quality of life .

Mental health disorders among infertile people have been postulated to stem from different causes. Hormonal treatment such as clomiphene citrate, often used in these individuals, has been implicated in the development of anxiety and sleep disturbances in women (18). Low self-esteem and feelings of loss of control of one's life have been implicated(19). Others include:

financial stress, pressure from family and friends, and the unpredictability associated with the treatment options and duration (20). Infertility has also been found to impact negatively on the affected couple's relationship, sexuality, spirituality, productivity at work, and relationship with others- all these contribute to their psychological distress (21).

Studies show that anxiety and depression reduce the chances of achieving a pregnancy, either spontaneously or through Artificial Reproductive Technology (ART) (22). Moreover, psychological distress among patients with infertility has been implicated as the main reason for discontinuing treatment.

CHAPTER TWO: LITERATURE REVIEW

2.1. Introduction

Among infertile individuals, generalized anxiety disorder and depression are the predominant mental health problems (16). Among the factors thought to contribute to these disorders are financial stress, pressure from family and friends, and the unpredictability associated with the treatment options and duration (20). A literature review of studies related to the subject matter published between 2004 and 2019 is presented in the section below.

2.2. Literature review

Literature review on the prevalence of generalized anxiety disorder and depression and their associated factors among patients with infertility

Shahraki et al. carried out a cross-sectional study in Iran between August 2015 and March 2016 and found that infertile men had a higher anxiety score ($p = 0.03$) and lower quality of life scores ($p = 0.03$) than fertile men. Depression was not found to be higher in men who were infertile compared to those who were fertile ($p < 0.06$). The study participants included 97 infertile men and 83 fertile men. The quality of life, generalized anxiety disorder and depression were assessed using the 36-item Short-form Health Survey (SF-36), Beck Anxiety Inventory (BAI), and Beck Depression Inventory (BDI) respectively (23).

Maroufizadeh et al. conducted a study on the prevalence of depression and anxiety among infertility patients in Iran between January 2014 and March 2015. The study was cross-sectional in nature. It had 1128 participants attending a referral infertility clinic. The tool of choice for data collection was The Hospital Anxiety and Depression Scale (HADS) (24), a validated tool for self-assessment of depression and generalized anxiety disorder. The study found prevalence rates of 49.6% for anxiety and 33% for depression (n=1128). Women were 26% more likely to develop symptoms of anxiety than men, while the presence of depression was not related to the sex of the patient (95% CI 0.84-1.42). A period of infertility exceeding 5 years was found to increase the risk of getting symptoms of anxiety by 51% and those of depression by 30%. There was no association between anxiety and elements such as previous abortions, age and the cause of infertility. In addition to this, there was no association between depression and age ($p=0.529$), history of abortion ($p=0.245$), and sex ($p=0.445$) (20) .

A cross-sectional study by Lakatos et al. was conducted in two private fertility centres and a public university gynaecology clinic in Hungary between September 2013 and September 2014. The study participants consisted of 134 nulliparous women with involuntary childlessness and 91 fertile women. The Fertility Problem Inventory (FPI), State-Trait Anxiety Inventory (STAI), as well as the BDI were used to collect data. Symptoms of anxiety and depression were more prevalent in the women who were involuntarily childless ($p<0.001$ for both depressive and anxiety). Among the infertile women, 44.8% had moderate to severe depression (n=134). Symptoms of the two conditions combined were more prevalent among infertile women in comparison to the fertile ones (37.3% vs 17.6% respectively). Among the infertile women, the presence of depression was more significant among those with a history of ART than those without it ($p<0.05$). Both groups of infertile women had an insignificant difference in trait-anxiety and infertility-related stress ($p=0.350$ and $p=1.96$ respectively). The study found an association between depression and age ($p<0.018$), social concern ($p<0.003$), sexual concern ($p<0.001$), and maternal relationship stress ($p<0.002$). Anxiety was significantly associated with factors such as age ($p<0.026$), social concern ($p<0.001$), financial stress ($p<0.005$), sexual concern ($p<0.002$), and maternal relationship stress ($p<0.011$) (25).

A cross-sectional study carried out by Joelsson et al. in Sweden, focusing on anxiety and depression among non-gravid women with sub-fertility, women who conceived through ART, and women who conceived spontaneously, found that symptoms of anxiety were more prevalent among non-gravid women with sub-fertility compared to those who conceived through ART and those who conceived spontaneously with a prevalence of 57.6%, 21.1% and 18.8% respectively. Depression were most prevalent among non-gravid women with sub-fertility compared to those who conceived through ART and those who conceived spontaneously; with a prevalence of 15.7%, 8.5% and 10.3%, respectively ($p=0.001$). After controlling for confounders, the prevalence of symptoms of depression was not statistically significant among non-gravid women with sub-fertility compared to the rest ($p=0.31$). Symptoms of anxiety were more prevalent among non-gravid women with sub-fertility compared to the rest after controlling for confounders ($p<0.001$). The study participants included 468 non-gravid women with sub-fertility, 143 who conceived through ART and 2972 who conceived spontaneously. Data collection tools used in the study were HADS for anxiety and Edinburgh Postnatal Depression Scale (EPDS) for depression, respectively (26).

A descriptive study carried out by Yang et al in China between November 2015 and March 2016 found a 20.8% prevalence of depression, a 7.8% prevalence of symptoms of anxiety, and a 15.4% prevalence of symptoms of the two combined (n=781). The participants were of the age 19 to 65, the average being 32.3 ± 5.6 years. Depression were more prevalent among those below 30 years of age while anxiety were more prevalent among those over 40years of age, the prevalence being 23.3% and 12.7% respectively. However, age was not found to be a statistically significant risk factor for depression ($p = 0.23$), anxiety ($p = 0.21$), or both ($p = 0.54$). The level of education was not associated with symptoms of depression ($p = 0.44$), anxiety ($p = 0.92$), or the two conditions combined ($p = 0.57$). Most of the participants (83%) in the study had attained secondary education and above. There was a relationship between concomitant conditions such as epididymal cysts, erectile dysfunction and varicoceles and depression (OR 1.47), and a combination of both anxiety and depression (OR 1.56). The duration of involuntary childlessness was discovered to influence depression (OR 1.52), anxiety (OR 3.94), and symptoms of both anxiety and depression (OR 1.02). The participants in the study were 781 men who were undergoing infertility treatment at an andrology clinic. The questionnaires used to collect data incorporated both the Six-Item State-Trait Anxiety Inventory-Short Form (STAI-6) and Mental Health Inventory-5 (MHI-5) (27).

Yusuf carried out a case-control study at a hospital in Pakistan between February and August 2015 found a 79% prevalence of depression and 70% for anxiety in individuals being managed for infertility (n=100). Both mental health disorders were found to be high irrespective of the level of education or occupation ($p<0.05$) among the infertile group. The Depression Anxiety Stress Scales (DASS) was the tool of choice for evaluation of stress and symptoms of anxiety and depression. The study had 200 participants: 100 women being managed for infertility in a teaching hospital and 100 fertile women as controls (28).

A study, cross-sectional in design, carried out from May to October 2015 by Abbasi et al. in Pakistan found a prevalence of 75% for anxiety and 31% for depression (n=100). The two conditions were not associated with age, period of infertility, and length of marriage ($p>0.05$). HADS was the tool of choice for evaluating symptoms of both psychiatric disorders. This study had 100 participants who were infertile women on fertility treatment (29).

A cross-sectional study carried out by Sezgin et al. from March to September 2011 in Turkey found no difference in the prevalence of symptoms of both anxiety and depression between infertile and fertile women ($p=0.131$ for anxiety and $p=0.574$ for depression respectively). More infertile women, however, had clinically significant anxiety compared to fertile women ($p=0.02$). The difference between infertile and fertile women as far as the proportion with clinically significant depression was not statistically significant despite the former having a higher proportion ($p=0.145$). The study participants consisted of 100 married infertile women attending an outpatient gynaecology clinic and 100 fertile controls. The tool of choice for evaluating symptoms of both anxiety and depression was HADS (30).

Alosaimi et al. carried out a study, cross-sectional in nature, in 3 infertility clinics in Saudi Arabia from January 2013 to September 2014 and found that anxiety and depression were the predominant mental health disorders among patients being managed for infertility. Depression had a prevalence of 21.7% while anxiety had a prevalence of 21.2% ($n=406$). The study participants were 206 female and 200 male individuals attending infertility clinics. Results of the study showed that 30% of men and 36.9% of women had mental health disorders. Among women, a low monthly income ($p=0.046$) and polygamy ($p=0.014$) were linked with psychiatric disorders. Among the men, a low monthly income was associated with psychiatric disorders; however, this was statistically insignificant ($p=0.069$). The Mini International Neuropsychiatry Interview (MINI) was used to evaluate psychiatric disorders (31).

A study, cross-sectional in design, conducted by Abass et al. within a fertility unit in a hospital in Ghana between December 2012 and April 2013 found a 62% prevalence of depression ($n=100$). Mild depression was found to be present in 40% of the women while moderate depression was present in 22% of them; none of them had severe depression. Majority of the women with depression had no formal education (38%). The higher the level of education, the less likely one was to get depressed. This, however, was statistically insignificant ($p=0.242$). Depression turned out to be more common among those with primary infertility than those with secondary infertility ($p=0.004$). There was a relationship between an increase in age and depression; this was statistically significant in women ≥35 years old ($p<0.001$). A duration of infertility ≥3 years was related to depression. Depression were assessed using the BDI. The study participants were 100 female individuals being managed for infertility in a hospital in Ghana (32).

A cross-sectional study by Yusuf et al. carried out in a hospital in Nigeria between June and December 2011 found a 17.3% and 11.1% prevalence of depression and generalized anxiety disorder (n=81). The only statistically significant factor associated with a risk of psychological distress was divorce ($p = 0.001$). The study participants were 81 men with an average age of 35.1 ± 6.7 years. All the participants were initially assessed using HADS and thereafter MINI was used to evaluate those with high scores (33).

In a descriptive study conducted in a fertility centre in Japan between February and April 2008, Ogawa et al. found an association between age, employment status, and unknown cause of infertility, and depressive and anxiety. Questionnaires incorporating the Self-rating Depression Scale (SDS) as well as HADS were administered to 83 women undergoing fertility testing or treatment. The participants had an average age of 34.5 ± 4.5 years. Women in their twenties had remarkably lower scores for depression compared to older women ($P<0.05$), indicating a significant association between an increase in age and depression. Women who were unemployed had higher scores for depression compared to those who were employed, but this was statistically insignificant ($P=0.07$). Women who had previously been treated for infertility scored higher for depression than women who had no prior treatment for infertility. Women who were aware of their spouses' infertility scored lower for anxiety than those who were unaware of the same ($p<0.05$) (34).

A cross-sectional nationwide Health 2000 survey by Klemetti et al. in Finland found that infertile men had an increased risk for mental disorders compared to fertile men but this was statistically insignificant. Infertile women had a 3.4 times higher risk of suffering from dysthymia compared to women who were fertile, as well as a 3 times higher risk for anxiety. The study recruited 2291 participants. Out of these, 338 had experienced infertility (20% of the women and 9% of the men) (35).

Sbaragli et al. conducted a case-control study between February 2006 and November 2006 in Italy. The participants consisted of 81 infertile couples, who were yet to begin fertility treatment, from an infertility centre and 70 controls from a gynaecology clinic. Interviews were carried out with the help of the Structured Clinical Interview for DSM-IV (SCID-I). Adjustment disorder with mixed anxiety and depressed mood was significant among infertile women compared to fertile women ($p=0.03$). Women had a higher prevalence of both anxiety

and depressed mood than men (p=0.03 and p=0.05 respectively). Maladjustment disorders with anxiety and depressed mood were more common in women with female factor infertility than those whose partners were infertile and the fertile arm (p=0.01). Adjustment disorder with depression was more common in those whose duration of infertility was >2 years than those whose infertility duration was <2 years (p=0.009) (36).

Chen et al. conducted a study, cross-sectional in design, between December 2002 and May 2003 in Taiwan and found a 17% and 9.8% prevalence of major depression and dysthymia, respectively, and a 23.2% prevalence of generalized anxiety disorder (n=112). A 15.2% prevalence of concomitant mood disorders and anxiety disorders was reported. There was no difference in anxiety/depression between those who had a history of ART and those preparing to undergo their first cycle of ART. Participants in the study were 112 women being managed for infertility at a fertility centre; some had a history of prior ART while others were yet to undergo ART. The participants were given HADS for self-reporting of symptoms of anxiety/depression, in addition to being subjected to an interview where a psychiatrist used the MINI tool for diagnosis of psychiatric disorders (37).

Ramezanzadeh et al. carried out a study, cross-sectional in nature, within a research centre related to reproductive health in Iran from January 2001 to January 2002, investigating the association between two psychiatric disorders (depression and anxiety) and factors such as the cause of infertility as well as the period of infertility. They found a 40.8% prevalence of depression and an 86.8% prevalence of anxiety (n=370). The cause of infertility was linked to depression(p=0.014), while no association was found for anxiety (p=0.485). The relationship between depression and duration of infertility treatment was statistically insignificant (p=0.048). Depressive and anxiety were more among the unemployed than the employed women. The education level was negatively correlated with symptoms of depression (p<0.001) and anxiety (p=0.003). The participants were 370 infertile women with an average age of 28 ± 5.37 years and an average period of infertility of 6.36 ± 4.18 years. Cattle Inventory was used to evaluate symptoms of anxiety while Beck Depression Inventory (BDI) was used to evaluate depression (38).

In summary, several studies show that generalized anxiety disorder and depression are prevalent among infertile individuals. An association between age, employment status,

unknown cause of infertility, financial stress, sexual concerns, social concerns, underlying medical illnesses, duration of infertility, and symptoms of anxiety and depression has been described in literature. The high prevalence of symptoms of the two psychiatric conditions among infertility patients underscores the need for mental health support in their management.

Table 1: Summary of literature review on the prevalence of generalized anxiety disorder and depression and their associated factors among patients with infertility

Author/ Year/Country	**Study title**	**Study design**	**Findings**
Shahraki et al. (2019) Iran	How Different are Men with Infertility-Related Problems from Fertile Men in Prevalence of Depression, Anxiety and Quality of Life?	Cross-sectional	• Infertile men had a higher anxiety score ($p = 0.03$) than fertile men. • Depression was not found to be higher in infertile men than fertile men ($p < 0.06$).
Maroufizadeh et al. (2018) Iran	The prevalence of anxiety and depression among people with infertility referring to Royan Institute in Tehran, Iran: A cross-sectional questionnaire study	Cross-sectional	• Mean age 31.37 ± 5.69 • Mean duration of infertility 5.62 ± 4.03 years • Prevalence rates of 49.6% for anxiety and 33% for depression. • Anxiety 26% more likely in women; no sex differences for depression. • 51% higher risk of getting anxiety and a 30% higher risk of developing depression if duration of infertility is longer than 5 years.
Lakatos et al. (2017) Hungary	Anxiety and depression among infertile women: a	Cross-sectional	• Mean duration of infertility 3.61 ± 3.08 years.

	cross-sectional survey from Hungary		• Depressive and anxiety were found to be higher among the infertile women ($p<0.001$ for symptoms of both). • 44.8% of infertile women had moderate to severe depression. • Depression more significant among those with a history of ART than those without ART ($p<0.05$).
Joelsson et al. (2017) Sweden	Anxiety and depression symptoms among sub-fertile women, women pregnant after infertility treatment, and naturally pregnant women	Cross-sectional	• Prevalence of anxiety among sub-fertile non-pregnant 57.6% compared to 21.1% and 18.8% among women who conceived after ART, and those who conceived spontaneously, respectively ($p<0.001$). • 15.7% prevalence of depression among the sub-fertile women compared to 8.5% and 10.3% among those who conceived after ART and those who conceived spontaneously, respectively ($p=0.001$). • Prevalence of depression among sub-fertile women not statistically significant compared to the rest after controlling for confounders ($p=0.31$). • Prevalence of anxiety among sub-fertile women statistically significant compared to the rest despite controlling for confounders ($p<0.001$).

Yang et al. (2017) China	Assessment on Occurrences of Depression and Anxiety and Associated Risk Factors in the Infertile Chinese Men	Descriptive	• Prevalence of depression was 20.8%, prevalence of anxiety was 7.8%, and the prevalence of both anxiety and depression was 15.4%. • High prevalence of depression (23.3%) in men below 30. • High prevalence of anxiety in men over 40 (12.7%). • No association between age and symptoms of depression, anxiety, or both ($p = 0.23$, $p = 0.21$, and $p = 0.54$ respectively). • No association between level of education and symptoms of depression, anxiety, or both ($p = 0.44$, $p = 0.92$, and $p = 0.57$ respectively). • Concomitant conditions were associated with a high risk of depression (OR 1.47), and symptoms of both anxiety and depression (OR 1.56). • Duration of infertility was a risk factor for symptoms of depression (OR 1.52), anxiety (OR 3.94), and a combination of the 2 (OR 1.02).
Yusuf (2016) Pakistan	Depression, anxiety and stress among female patients of infertility: a case control study	Case-control	• Prevalence of depression among infertility patients 79%. • Prevalence of anxiety among infertility patients 70%. • Depression and anxiety were found to be high irrespective of

			level of education or occupation ($p<0.05$) among the infertile group
Abbasi et al. (2016) Pakistan	Depression and anxiety in Pakistani infertile women	Cross-sectional	• Prevalence of anxiety 75%. • Prevalence of depression 31%. • No association between anxiety/depression and age, duration of infertility, and length of marriage ($p>0.05$).
Sezgin et al. (2016) Turkey	Disability, psychiatric symptoms, and quality of life in infertile women: a cross-sectional study in Turkey	Cross-sectional	• No difference in the presence of anxiety/depression between infertile and fertile women ($p=0.131$ for anxiety and $p=0.574$ for depression respectively). • Higher proportion of infertile women with clinically significant anxiety than controls ($p=0.02$). • Clinically significant depression higher in infertile women but not statistically significant ($p=0.145$).
Alosaimi et al. (2015) Saudi Arabia	Psychiatric disorders among infertile men and women attending three infertility clinics in Riyadh, Saudi Arabia.	Cross-sectional	• Mean age 31.5 for women and 35.4 for men. • Prevalence of depression 21.7%. • Prevalence of anxiety 21.2%. • Among the women, a low monthly income ($p=0.046$) and polygamy ($p=0.014$) were found to be associated with psychiatric disorders. • Among the men, a low monthly income was associated with psychiatric disorders but this was

			not statistically significant (p=0.069).
Abass et al (2014) Ghana	A survey on depression among infertile women in Ghana	Cross-sectional	• Mean age 30.5 years • Prevalence of depression 62% • Majority of women with depression had no formal education (38%). • Depression more common in those with primary infertility than those with secondary infertility (p=0.004). • Statistically significant association between age ≥35 and depression (p<0.001). • A duration of infertility ≥3 years associated with a higher likelihood of depression
Yusuf et al. (2012) Nigeria	Socio-demographic correlates of psychological distress among male patients with infertility in Zaria, Nigeria.	Cross-sectional descriptive	• Mean age of 35.1 ± 6.7 years • 17.3% of the respondents were found to have depression. • 11.1% of the respondents were found to have a generalized anxiety disorder. • The only statistically significant factor associated with a risk of psychological distress was divorce (p = 0.001).
Ogawa et al. (2011) Japan	Evaluation of factors associated with the anxiety and depression of female infertility patients	Descriptive	• Mean age was 34.5 ± 4.5 years. • Women in their twenties had lower depression scores than women ≥ 35 (p<0.05).

			• Unemployment associated with higher depression scores although not statistically significant (p=0.07). • Previous history of infertility treatment associated with depression. • Unknown aetiology of infertility associated with anxiety (p<0.05)
Klemetti et al. (2010) Finland	Infertility, mental disorders and well-being- a nationwide survey	Cross-sectional survey	• Mean age of 36.6 ± 0.6 for infertile women, and a mean of 37.9± 0.8 for infertile men. • Increased risk of mental disorders among infertile men but not statistically significant. • Infertile women were 3.4 times more likely to suffer from dysthymia than fertile women, and 3 times more likely to suffer from anxiety than fertile women.
Sbaragli et al. (2008) Italy	Infertility and psychiatric morbidity	Case-control	• Adjustment disorder with mixed anxiety and depressed mood more likely in the infertile arm than fertile arm (p=0.03). • Both anxiety and depressed mood were higher in women than men (p=0.03 and p=0.05 respectively). • Maladjustment disorders with anxiety and depressed mood more common in women with female factor infertility than those with infertile partners and controls (p=0.01).

			• Adjustment disorder with depression more common in those whose duration of infertility was >2 years than those whose infertility duration was <2 years (p=0.009).
Chen et al. (2004) Taiwan	Prevalence of depressive and anxiety disorders in an assisted reproductive technique clinic	Cross-sectional	• Prevalence of major depression 17%. • Prevalence of dysthymia 9.8% • Prevalence of generalized anxiety disorder 23.2%. • Prevalence of concomitant mood and anxiety disorders 15.2%. • No difference in anxiety/depression between those who had a history of ART and those preparing to undergo ART for the first time.
Ramezanzadeh et al. (2004) Iran	A survey of relationship between anxiety, depression and duration of infertility	Cross-sectional	• Mean age 28 ± 5.37 and mean duration of infertility 6.36 ± 4.18 • 40.8% prevalence of depression and an 86.8% prevalence of anxiety. • Association between the cause of infertility and the presence of depression (p=0.014), no association was found for anxiety (p=0.485). • No relationship between depression and duration of infertility (p=0.048). • Negative correlation between the level of education and symptoms

			of depression and anxiety ($p<0.001$ and $p=0.003$ respectively)

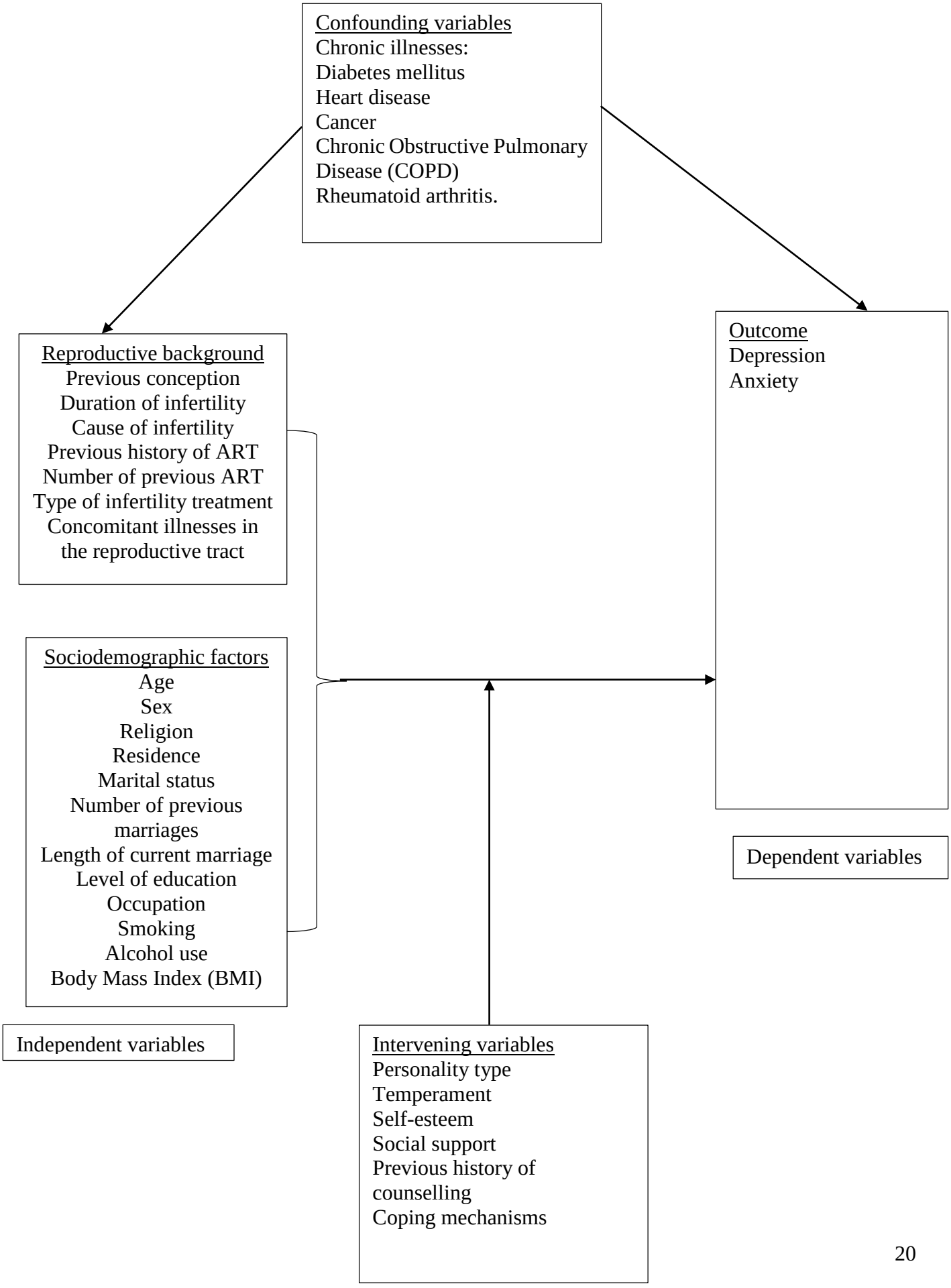
2.3. Conceptual framework

The relationship between the dependent and independent variables within this study is illustrated in the conceptual framework below (Figure 1.1). The aim of the study was to determine the prevalence and factors associated with symptoms of depression and generalized anxiety disorder among patients being managed for infertility at two fertility centres in Nairobi. The independent variables were sociodemographic factors and reproductive background. Sociodemographic factors included age, sex, religion, residence, marital status, number of previous marriages, length of current marriage, level of education, occupation, smoking, alcohol use, and BMI. The reproductive background consisted of cause and duration of infertility, previous conception, previous history of ART, number of previous ART, type of infertility treatment, and concomitant illnesses in the reproductive tract.

The dependent variables were depressive and anxiety.

The intervening variables were: personality type, temperament, self-esteem, social support, previous history of counselling, and coping mechanisms. The confounding variables were chronic illnesses that are associated with infertility and mental health disorders i.e. depression and anxiety. These conditions include: diabetes mellitus, heart disease, cancer, Chronic Obstructive Pulmonary Disease (COPD), and rheumatoid arthritis.

Figure 1. 1: A diagrammatic representation of the conceptual framework



2.4. Problem statement

WHO estimates that infertility affects 1 in 4 couples in low- and middle-income countries. Infertility has an influence on all facets of the affected individual's life and has been found to cause mental health disorders, particularly generalized anxiety disorder and depression. Psychological distress forms part of the reasons as to why infertile couples discontinue care. Furthermore, the two psychiatric disorders have been found to reduce the chances of conception, either spontaneously or through ART. Understanding the prevalence and factors linked to the two psychiatric disorders among patients with infertility, particularly those attending a fertility clinic with ART services, is key in improving their follow up and outcomes.

2.5. Justification

In 1948, the right to start one's own family and determine the size of the same was recognized as being fundamental in meeting their reproductive health needs (39). However, little has been done to address this since then. The global focus has, instead, been on curbing population growth through emphasis on contraceptives. ICPD at 25, which took place in Nairobi in 2019, included counselling as well as services for infertility, including diagnostics and assisted reproduction, in the comprehensive package of quality Sexual and Reproductive Health (40).

That notwithstanding, ART is unavailable in the public health sector in Kenya. This is despite the WHO estimate of 1 in every 4 couples in low- and middle-income countries being affected by infertility. This study was conducted in two private fertility centres so as to include those preparing to undergo, those who were undergoing ART at the time, and those who had already undergone ART. This was done to enrich the quality of the data emanating from this study.

Generalized anxiety disorder and depression are the predominant mental health problems among infertile individuals (16). This study focused on the two conditions owing to their magnitude as described in literature. Health practitioners in reproductive health should be cognizant of the two and their role in the continuity of care as well as the chances of achieving a pregnancy (the goal of every fertility treatment) among these patients (22). Psychological distress has been cited as the main reason for discontinuing ART even in countries where ART is covered by insurance or sponsored by the state (21).

Despite evidence showing the association between infertility and mental health disorders, counselling is not routinely done for infertility patients in Kenya. This study has provided data to identify those at high risk of getting mental health disorders. It has also provided insight on what to include in the psychological support for these patients.

The data obtained from this study highlights the need for incorporating mental health support in the management of infertility in Kenya and influence policy on the same.

2.6. Research question

What is the prevalence of generalized anxiety disorder and depression as well as their associated factors among patients undergoing treatment for infertility at two fertility centres in Nairobi between January and March 2022?

2.7. Research objectives

2.7.1. Broad objective

To establish the prevalence of generalized anxiety disorder and depression as well as their associated factors among patients undergoing treatment for infertility at two fertility centres in Nairobi between January and March 2022.

2.7.2. Specific objectives

Among the patients being treated for infertility at two fertility centres in Nairobi:

1. To determine the prevalence of generalized anxiety disorder.
2. To establish the prevalence of depression.
3. To identify the factors associated with generalized anxiety disorder.
4. To demonstrate the factors associated with depression.

2.8. Significance and anticipated output

Data emanating from this study shall help improve on the care of couples affected by infertility as expounded in the justification section 2.5.

CHAPTER THREE: MATERIALS AND METHODS

3.1. Study design

The study employed a cross-sectional design with a sub-group analysis.

3.2. Study site

This study was carried out in two private fertility centres in Nairobi: Fertility Point and Creation Fertility Centre. Both centres offer fertility treatment, including ART. Some of the ART options offered in both centres include Intrauterine Insemination (IUI) and Intracytoplasmic Sperm Injection (ICSI), as well as sperm aspiration techniques such as Percutaneous Epididymal Sperm Aspiration (PESA) and Testicular Sperm Aspiration (TESA). Both centres have a gamete donation programme. Other services include egg vitrification, assisted hatching, and surrogacy. Patients attending the two facilities come from different parts of the country, as well as from other countries.

Fertility Point is an international organization that has different branches across the world. In Kenya, Fertility Point is located at Fortis Suites on Hospital Road in Upper Hill, Nairobi. The centre was established three years ago. The average number of patients seen in a day is 15. This number includes repeat clients, surrogates and those in the egg/sperm donation programme. The centre has a staff of 21. The centre is staffed by an IVF specialist, gynaecologist, medical officer, nurses with IVF lab experience, pharmaceutical technologist, lab technologist, medical records officer, anaesthetist, andrologist, embryologist, and non-clinical staff (biomedical engineer, health care administrator, customer service staff, business development officers, human resource officer, accountants, cashiers, and hotel services officers). In addition to this, there are external IVF specialists from different regions in Kenya who carry out ART procedures in the facility. Counselling is not routinely done as part of management of infertility.

Creation Fertility Centre is located at Prof. Nelson Awori Centre on Ralph Bunche Road, Nairobi. The centre was founded one year ago. The average number of patients seen in a day is 5. This number includes repeat clients, surrogates and those in the egg/sperm donation programme. The centre has a staff of four, comprising an administrator, administrative assistant, nurse, and andrologist. In addition to this, there are five IVF specialists affiliated to

the centre. There are 4 anaesthetists, 1 embryologist, 1 sonographer, 2 counsellors, and 3 theatre nurses on part time basis. Counselling is mainly done for patients who need a surrogate, hence not part of routine care.

3.3. Study population

The study consisted of men and women undergoing treatment for infertility at two private fertility centres in Nairobi between January and March 2022. A pro rata allocation of patients was done. The allocation was as follows:

Number of patients seen at Fertility Point in a day: 15

15 x 6 = 90 patients per week

90 x 4 = 360 patients in a month

Number of patients seen at Creation Fertility Centre in a day: 5

5 x 6 = 30 patients per week

30 x 4 = 120 patients in a month

Therefore:

Number of patients who were recruited in the study from Fertility Point:

$$\frac{360}{360 + 120} \times 100 = 75\%$$

$$\frac{75}{100} \times 124 = 93\ patients$$

Number of patients who were recruited from Creation Fertility Centre:

$$\frac{120}{36 + 120} \times 100 = 25\%$$

$$\frac{25}{100} \times 124 = 31\ patients$$

Therefore, 93 patients were recruited from Fertility Point and 31 patients were recruited from Creation Fertility Centre, respectively.

More women than men are seen in each centre. Approximately 1 in every 6 patients are men. A pro rata allocation of men and women to be recruited in the study was done as follows:

Number of men: $\frac{1}{1+5} \times 124 = 21$ men

Number of men from Fertility Point:

$$\frac{75}{100} \times 21 = 16\ men$$

Number of men from Creation Fertility Centre:

$$\frac{25}{100} \times 21 = 5\ men$$

Number of women: $\frac{5}{1+5} \times 124 = 103$ women

Number of women from Fertility Point:

$$\frac{75}{100} \times 103 = 77\ women$$

Number of women from Creation Fertility Centre:

$$\frac{25}{100} \times 103 = 26\ women$$

Therefore, 103 women and 21 men were recruited into the study. Of these, 77 women were from Fertility Point while 26 were from Creation Fertility Centre. Among the men, 16 were recruited from Fertility Point while 5 were recruited from Creation Fertility Centre.

3.4. Study variables

The dependent variables in this study included depressive and anxiety. The independent variables were sociodemographic factors and reproductive background. Sociodemographic factors included age, sex, religion, residence, marital status, number of previous marriages, length of current marriage, level of education, occupation, smoking, alcohol use, and BMI. The

reproductive background consisted of cause and duration of infertility, previous conception, previous history of ART, number of previous ART, type of infertility treatment, and concomitant illnesses in the reproductive tract. The intervening variables were: personality type, temperament, self-esteem, social support, previous history of counselling, and coping mechanisms. The confounding variables were chronic illnesses comprising diabetes mellitus, heart disease, cancer, Chronic Obstructive Pulmonary Disease (COPD), and rheumatoid arthritis.

Table 2: Study variables of patients being managed for infertility in two fertility centres in Nairobi

Objective	**Variables**	**Outcome**	**Source of data**
1. To determine the prevalence of anxiety.	Cases of anxiety over the total sample size.	Prevalence of anxiety.	The State-Trait Anxiety Inventory (STAI) tool.
2. To determine the prevalence of depression.	Cases of depression over the total sample size	Prevalence of depression	The Beck Depression Inventory (BDI)
3. To determine the factors associated with depression.	Age Sex Religion Level of education Occupation Residence Marital status	Factors of Depression	Questionnaires

	Number of previous marriages Length of current marriage BMI Smoking Alcohol use Concomitant illnesses in the reproductive tract Duration of infertility Cause of infertility Previous history of ART Type of fertility treatment		
4. To determine the factors associated with symptoms of anxiety	Age Sex Religion Level of education Occupation Residence	Factors of anxiety	Questionnaires

	Marital status Number of previous marriages Length of current marriage BMI Smoking Alcohol use Concomitant illnesses in the reproductive tract Duration of infertility Cause of infertility Previous history of ART Type of fertility treatment		

3.5. Inclusion criteria

The inclusion criteria was as follows:

- Patients being managed for infertility
- Age >19years (able to give consent and ≥1 year of regular unprotected coitus above the age of 18 years)

3.6. Exclusion criteria

The exclusion criteria was as follows:

- Patients with other chronic illnesses: diabetes mellitus, cancer, heart disease, COPD and rheumatoid arthritis.

3.7. Sample size determination and sampling techniques

3.7.1. Sample size determination

Calculation of the sample size was done using the Fisher's formula as shown below:

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Whereby,

n = Represented the sample size that was desired

Z = Represented a value within the normal distribution that corresponds to the confidence level that was desired

(Z=1.96 for 95% CI)

P = Represented the true proportion that was expected (approximated at 21.7% based on a study by Alosaimi et al. (2015) in Saudi Arabia, which reported a 21.7% prevalence of depression among the study participants.)

d = desired precision (0.05)

$$n_0 = \frac{1.96^2 x\ 0.217(1-0.217)}{0.05^2} = 261$$

At the time, in private fertility centres, 3 patients were seen with infertility per day. Per month, those eligible using the inclusion criteria of the study was approximately 20, and this amounted to 240 patients annually. Adjusting the sample size for finite populations less than 10,000.

$$nf = \frac{n_0}{1 + \frac{n_0 - 1}{N}} = \frac{261}{1 + \frac{261 - 1}{240}} = 124$$

The requisite sample size for this study was 124 individuals being managed for infertility.

3.7.2. Sampling techniques

Convenience sampling of patients attending the two private fertility centres was done till the desired number of 124 individuals was achieved.

3.8. Tool for collection of data

A questionnaire comprising sociodemographic factors, reproductive background, and depressive/anxiety self-reporting scales was used to collect data. The questionnaire is presented in Appendix II. Sociodemographic information included age, sex, residence, religion, marital status, number of previous marriages and length of current marriage, level of education, occupation, history of cigarette smoking and use of alcohol, and BMI. The information within the reproductive background consisted of previous conception, duration and cause of infertility, previous history of ART, number of previous ART, type of infertility treatment (medical/surgical/ART), and concomitant illnesses in the reproductive tract (e.g. vaginismus, varicoceles, erectile dysfunction).

The Beck Depression Inventory (BDI) has been validated for self-reporting of depression. It has 21 multiple choice items, each with 0-3 points. The total score is a measure of the extent of depression, where 0-16 is considered to be normal, 17-27 considered to be mild depression, 28-34 considered to be moderate depression, and 35-63 considered to be severe depression (38). The BDI is noted to be highly sensitive and valid, and has a high internal consistency (41).

The State-Trait Anxiety Inventory (STAI) has been validated as a tool for assessing both state and trait aspects of anxiety. The longer version of STAI has 40 elements, the first half focuses on the state aspect while the latter half focuses on the trait aspect (42). STAI is described as having good internal consistency and reliability (43). State anxiety refers to the patient's present anxiety disposition which is dependent on external factors whereas trait anxiety refers to their susceptibility to anxiety depending on personality, temperament and past experiences. Shorter versions of STAI have been developed in order to reduce the time taken to fill it (44) as well as to allow its use in patients who are severely unwell (45). These include the 20 item STAI which will be used in this study (46). A score of less than 45 indicates lack of anxiety, 45-53 indicates mild anxiety whereas a score of >53 indicates severe anxiety (25). The shorter versions of STAI have been found to be reliable (45). The data collection tool in this study included the 20-item STAI in order to shorten the time the patients required to fill it and maintain reliability of the data.

Reliability

Reliability refers to the consistency of results measured by a data collection tool. In this study, the reliability of the data collection instruments, BDI and STAI, was measured by using the

Cronbach's alpha to check for internal consistency. Internal consistency focuses on the respondents' consistency in answering questions within a questionnaire. For example, the BDI is a tool used for the assessment of depression. One would expect, in this case, that if a patient has depression, their responses would be corresponding throughout the questionnaire. Once the data collection process came to an end and the data was analyzed, the items in each data collection instrument was split into two halves after which a score for each half was calculated. The correlation between the scores for each half was then explored. The Cronbach's alpha was found to be .92, ensuring the reliability of the data. A Cronbach's alpha value of .70 to .79 is indicative of a satisfactory internal consistency, a value of .80 to .89 is indicative of a good internal consistency, while a value of .90 to .99 is indicative of an excellent internal consistency.

Validity

Validity refers to the accuracy with which a data collection instrument measures what it is meant to measure. There are several aspects of validity including face validity, content validity and criterion validity. Face validity refers to the respondents' perception of how well the instrument covers the subject being measured. Content validity refers to how well the instrument represents the subject being measured according to observers or experts. Criterion validity refers to the correlation between scores in the instrument being used and a different instrument which covers the same subject.

BDI has already been found to be a valid tool in screening and diagnosing depression in health facilities in Kenya (47). In that case, it was not tested in this study. STAI has also been used in studies in Kenya.

Pilot test

In order to increase the reliability and validity of the two instruments used in this study, BDI and STAI, a pilot test was conducted. This was done in the infertility clinic in Kenyatta National Hospital (KNH) by the principal investigator. A convenient sample of 10 patients being managed for infertility in this clinic was recruited. These patients were given questionnaires incorporating BDI and STAI for self-reporting of depressive and anxiety. The average time taken to fill each questionnaire and any difficulties in understanding or responding to the questions were noted. This information was used to improve the questionnaire before administering it to the actual study participants. The pilot test was conducted in KNH to avoid sampling the same patients who would be recruited into the study.

3.9. Procedure for data collection

Collection of data commenced once the KNH-UoN Ethics Committee, Fertility Point and Creation Fertility Centre granted their approval. The patients were conveniently selected. The Principal Investigator (PI) and research assistants ensured that the selected patients met the inclusion criteria after which they obtained consent from them and gave out the questionnaires. Each patient was informed that the estimated time to complete the questionnaire would be about ten minutes. The questionnaires had the BDI and STAI scales for self-reporting of depressive/anxiety. To enhance confidentiality, the study participants filled the questionnaires in a separate room instead of doing so in the waiting area.

The research assistants in this study included a medical officer and two nurses working at Fertility Point, as well as a nurse working at Creation Fertility Centre. The research assistants, by virtue of working in a fertility centre, were familiar with the management of infertility hence taking them through the details of the study was not difficult. The study did not interfere with their schedule since the questionnaires were self-administered hence they spent very little time with the study participants.

In order to reduce the risk of spread of COVID-19 infection during the data collection, the principal investigator discussed some measures to be observed with the research assistants. These measures included: ensuring that patients and research assistants washed or sanitized their hands when they arrived at the facility as well as before and after handling the questionnaires, ensuring that everybody within the fertility centres wore a mask correctly, periodic decontamination of surfaces with 0.5% chlorine, encouraging cough etiquette among the patients and members of staff, avoiding shaking hands, and maintaining the one metre social distance between individuals.

3.10. Quality assurance and control

Before the data collection process began, a pilot test of the study instruments was conducted. This was able to point out the challenges associated with answering the questions. The questionnaires were then adjusted before being administered to the actual study participants.

The research assistants were taken through what the study entailed, including the inclusion and exclusion criteria as well as obtaining consent. This helped to reduce errors during data collection. They then proceeded to give the questionnaires to patients for self-reporting of anxiety and depression after obtaining consent and ensuring that they met the inclusion criteria.

The reliability, validity, high sensitivity and internal consistency of the standardized tools for data collection (BDI and STAI) enhanced the integrity of data collected in this study.
The principal investigator counterchecked the data collected for accuracies and consistencies to ensure they met the standards required of this research. The identification of potential sources of error before data collection began helped mitigate errors thus maintain the integrity of data. For example, the research assistants were asked to ensure that study participants were told to complete all the items in the questionnaire in order to get valid results.
A clear documentation of the data collection process as well as storage, handling and analysis of data has been done as part of quality assurance.

3.11. Data management

The collected data was kept locked and confidential, and was only be accessed by the statistician and principal investigator of the study.
Once data was collected, Epi info 3.5.4 was used to enter data. Entered data was converted to a password protected Microsoft Excel sheet. Only the principal investigator and the authorized biostatistician were allowed to access the information. Preservation of data was done until it was analyzed, presented and archived.

3.12. Data analysis

Data was checked for completeness and free of error prior to entry into Epi info 3.5.4. The data was converted to Microsoft Excel Spreadsheet after which it was analyzed using the Statistical Package for Social Science (SPSS) version 26.0.
Analysis of the patients' sociodemographic and reproductive characteristics was done, after which the categorical data was presented in the form of percentages and frequencies while continuous data was presented as means with standard deviations.
The prevalence of generalized anxiety disorder and depression was calculated as a proportion of those patients with depressive/anxiety and reported as percentages. Factors associated with generalized anxiety disorder and depression were subjected to Pearson's Chi-square tests, after which a multivariable analysis incorporating logistic regression was done on those that were statistically remarkable.
Calculation of odds ratio and 95% confidence intervals was done, and all statistical tests were considered significant where $p < 0.05$.

Table 3: A summary of the data analysis

Objective		**Analysis**
1	Prevalence of anxiety	$\frac{Number\ of\ patients\ with\ anxiety\ symptoms}{Total\ number\ of\ patients}\ x100\%$
2	Prevalence of depression	$\frac{Number\ of\ patients\ with\ depressive\ symptoms}{Total\ number\ of\ patients}\ x100\%$
3	Factors associated with anxiety	Bivariate analysis using the Chi-square test and t-test for categorical and continuous variables respectively to obtain odds ratios and corresponding 95% confidence intervals. P values <0.05 were considered to be statistically significant. Statistically significant variables were subjected to a multivariate analysis using logistic regression models to obtain adjusted odds ratio and corresponding 95% confidence intervals.
4	Factors associated with anxiety	Same as above

3.13. Data presentation and dissemination

Analysed data was presented in written reports, frequency tables, pie charts, and graphs. Once the report was compiled, the data was presented to the Department of Obstetrics and Gynaecology, University of Nairobi as well as the two study sites. Data dissemination will also be carried out in conferences, professional groups and meetings, and a manuscript shall be published in a peer reviewed journal.

3.14. Ethical considerations

This research underwent ethical review and approval at the KNH-UON ERC. The principal investigator also sought authorization from Fertility Point and Creation Fertility Centre before data collection began (Appendix IV). Principles of confidentiality and privacy of

information was maintained throughout the research process. Patients' data was kept confidential at all data collection, abstraction, processing, and analysis stages. Data was anonymized and key patient identifiers like names, residence and age among others were de-identified.

Patients who were found to have high scores on the BDI and STAI scales were advised on the need for psychiatric review and were referred to the Department of Mental Health, Kenyatta National Hospital for treatment and follow-up. However, most patients opted to undergo counselling at their facilities of choice. In addition to this, some patients declined the option of referral and were counselled by the principal investigator.

Anonymity and Confidentiality: The PI also maintained anonymity and confidentiality by using non-identifiers such as codes that could not link a participant with the information provided during the study. The information obtained was solely for the purpose of this study and improving the implementation of service integration policy and not to divulge personal information to the public. Recorded data will be under custody of the principal investigator until validation within one year after which the data will be destroyed.

The principal investigator followed the ethical guideline provided by the KNH/UoN ERC in order to observe and sustain moral values related to the extent to which research methods adhere to legal, professional and sociological obligations.

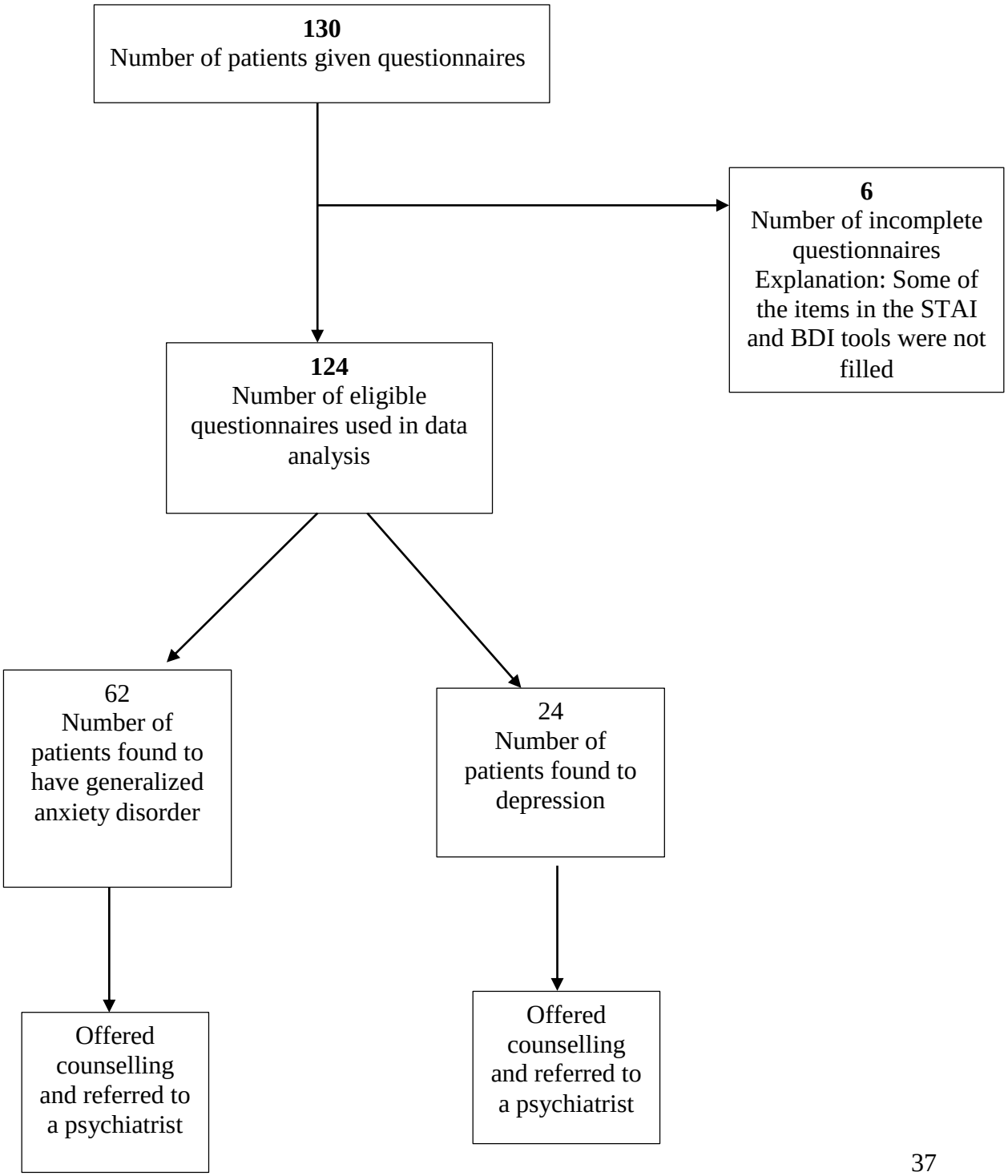
CHAPTER FOUR: RESULTS

4.1. Introduction

A total of 124 patients being managed for infertility at two fertility centres in Nairobi participated in the study.

4.2. Study flow chart

Figure 1. 2: A diagrammatic representation of the study flow of patients being managed for infertility at two fertility centres in Nairobi between January and March 2022



Between the 1st of January 2022 and the 31st of March 2022, 130 patients being managed for infertility at two fertility centres in Nairobi were recruited into the study after meeting the eligibility criteria and giving consent. The patients were given questionnaires to fill. Six questionnaires were excluded because of missing responses in the BDI and STAI section. Data from the 124 questionnaires was analysed and 62 patients were found to have generalized anxiety disorder while 24 were found to have depression. These patients were counselled by the principal investigator and referred to a psychiatrist.

4.3. Sociodemographic characteristics

This section describes the sociodemographic characteristics of the study participants. The mean age of the study participants was 37 ± 6.21 years. A majority of the participants were female (83%), Christians (94%), married (94%), employed (68%), urban dwellers (73%) and obese (36%). Most of them had not been married before (59%) and most had tertiary education (90%). A minority of them were smokers (2%) and alcohol consumers (20%). The average length of marriage was 8 ± 5.11 years. This is shown in Table 3.4 below.

Table 4: A table showing the sociodemographic characteristics of patients being managed for infertility at two fertility centres in Nairobi between January and March 2022 (n=124)

		Frequency (n)	Percentage (%)
Age (Mean ± SD)		37 ± 6.21	
Age groups	20 - 25	6	5%
	26 - 30	8	6%
	31 - 35	31	25%
	36 - 40	40	32%
	>40	39	31%
Gender	Female	103	83%
	Male	21	17%
Religion	Christian	116	94%
	Muslim	8	6%
Residence	Rural	34	27%
	Urban	90	73%
Marital status	Single	5	4%
	Married	117	94%
	Divorced/Widowed	2	2%
Previous Marriage	No	73	59%
	Yes	51	41%
Length of current marriage in years (Mean ± SD)		8 ± 5.11	
Level of education	None	1	1%
	Primary	1	1%
	Secondary	10	8%
	Tertiary	112	90%
Occupation:	Unemployed	2	2%
	Self-employed	38	31%
	Employed	84	68%
Smoking	No	122	98%
	Yes	2	2%
Alcohol use	No	99	80%
	Yes	25	20%
BMI	<20	4	3%
	20 - 24.9	36	29%
	25 - 29.9	39	31%
	>30	45	36%

4.4. Reproductive background

This section describes the reproductive background of the study participants. Primary infertility was the most common type of infertility (56%). The mean duration of infertility was 6 ± 4.34 years. Female factor was the predominant cause of infertility (40%). Most of the participants

were ART naive (63%). ART was the most common treatment modality (55%). Majority of the patients did not have a concomitant illness in the reproductive tract (90%).

Table 5: A table showing the reproductive characteristics of patients being managed for infertility at two fertility centres in Nairobi between January to March 2022 (n=124)

		Frequency (n)	**Percentage (%)**
Previous conception	No	70	56%
	Yes	54	44%
Duration of infertility in years (Mean ± SD)		6 ± 4.34	
Cause of infertility	Unexplained	47	38%
	Male factor	14	11%
	Female factor	50	40%
	Both male and female	13	10%
previous history of ART (IUI/IVF/ICSI)	No	78	63%
	Yes	46	37%
Type of fertility treatment	Oral drugs	40	32%
	ART (IUI/IVF/ICSI)	68	55%
	Surgery	16	13%
Concomitant illness in the reproductive tract	No	112	90%
	Yes	12	10%

4.5. Prevalence of generalized anxiety disorder and depression

Generalized anxiety disorder were screened using STAI. A score of <45 was classified as no anxiety, 45-53 as mild anxiety and >53 as severe anxiety (25). Symptoms of depression were screened using BDI where a score of 0-16 was considered to be normal, 17-27 was considered to be mild depression, 28-34 was considered to be moderate depression, and 35-63 was considered to be severe depression (38).

The prevalence of generalized anxiety disorder was found to be 50% as shown in Table 3.6. Of those who had symptoms of anxiety, 30% had mild anxiety and 20% had severe anxiety.

The prevalence of depression was found to be 19% as shown in Table 3.6. Of those who had depression, 10% had mild depression, 4% had moderate depression and 5% had severe depression.

Table 6: A table showing the prevalence of generalized anxiety disorder and depression and among patients being managed for infertility in two fertility centres in Nairobi between January and March 2022 (n=124)

		Frequency (n)	Percentage (%)
Depression	Yes	24	19%
	No	100	81%
Anxiety	Yes	62	50%
	No	62	50%

Figure 1. 3: A pie chart showing the prevalence of generalized anxiety disorder among patients being managed for infertility in two fertility centres in Nairobi between January and March 2022 (n=124)

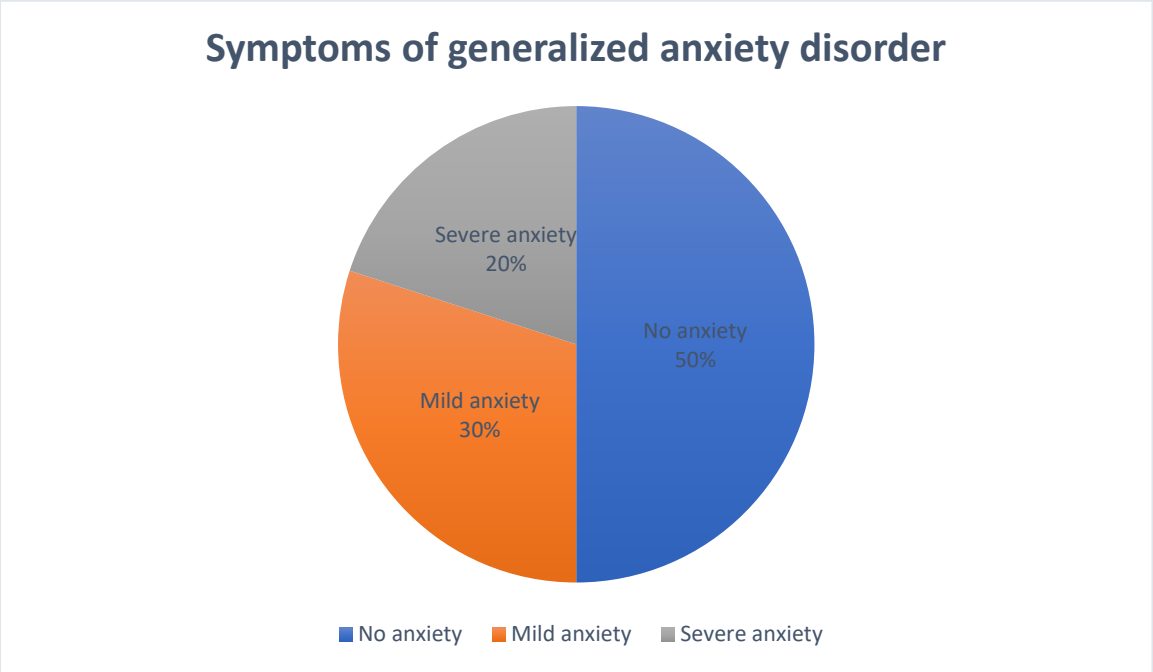
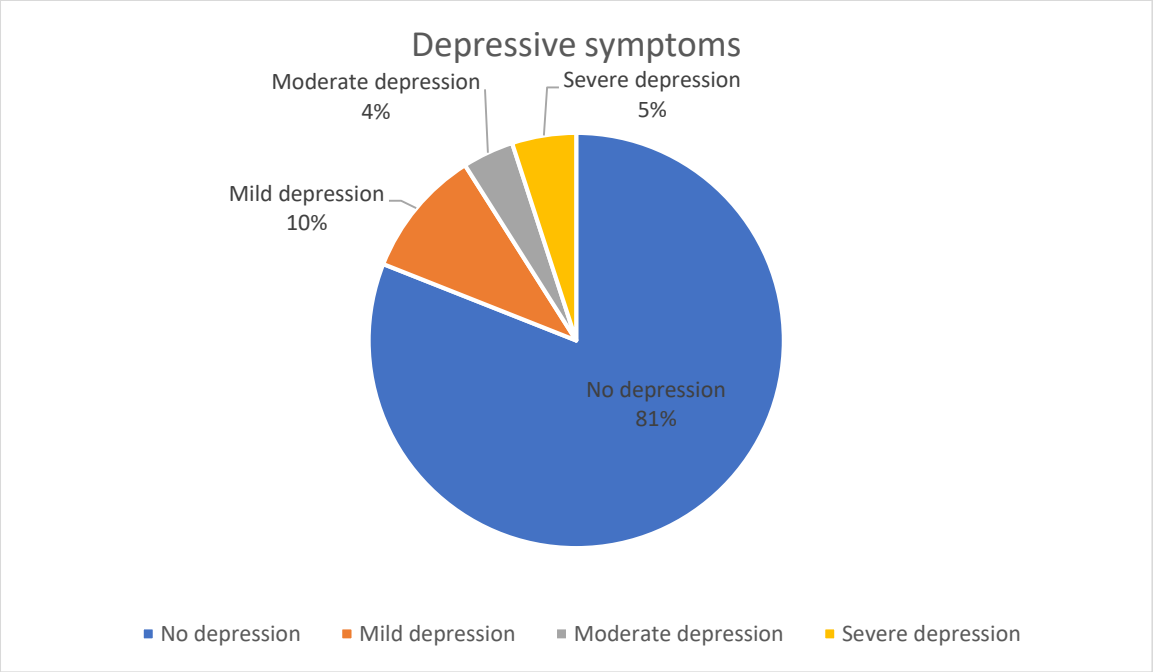


Figure 1. 4: A pie chart showing the prevalence of depression among patients being managed for infertility in two fertility centres in Nairobi between January and March 2022 (n=124)



4.6. Sociodemographic factors associated with generalized anxiety disorder

Sociodemographic factors were subjected to a bivariate analysis to establish the association between them and generalized anxiety disorder. The factors found to be associated with these symptoms were: previous marriage (p=0.007, OR 2.78, 95% CI 1.33,5.84) and depression (p<0.001, OR 10.07, 95% CI 2.82,36.00).

Age was not found to be associated with generalized anxiety disorder (p=0.49, AOR 1.02, 95%CI 0.96,1.08). This was the case even after classifying the patients into different age groups as shown in the table below. Gender, religion, residence, marital status, length of current marriage, level of education, occupation, smoking, alcohol use and BMI had no relationship with generalized anxiety disorder.

Table 7: A table showing the sociodemographic factors associated with generalized anxiety disorders among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		Anxiety			Bivariate (unadjusted)	
		No N=62	**Yes N=62**	**P-value[1]**	**OR (95%CI)**	**P-value[2]**
Age (Mean ± SD)		37 ± 6.54	38 ±5.89	0.49	1.02(0.96,1.08)	0.49
Age groups	20 - 25	4(6%)	2(3%)	0.817	0.53(0.09,3.22)	0.49
	26 - 30	5(8%)	3(5%)		0.63(0.13,3.02)	0.564
	31 - 35	14(23%)	17(27%)		1.28(0.50,3.29)	0.611
	36 - 40	19(31%)	21(34%)		1.16(0.48,2.81)	0.737
	>40	20(32%)	19(31%)		Ref	
Gender	Female	51(82%)	52(84%)	0.811	1.12(0.44,2.87)	0.811
	Male	11(18%)	10(16%)		Ref	
Religion	Christian	57(92%)	59(95%)	0.717	Ref	
	Muslim	5(8%)	3(5%)		0.58(0.13,2.54)	0.469
Residence	Rural	13(21%)	21(34%)	0.107	Ref	
	Urban	49(79%)	41(66%)		0.52(0.23,1.16)	0.11
Marital status	Single	3(5%)	2(3%)	1	Ref	
	Married	58(94%)	59(95%)		1.53(0.25,9.47)	0.65
	Divorced/Widowed	1(2%)	1(2%)		1.50(0.06,40.63)	0.81
Previous Marriage	No	44(71%)	29(47%)	**0.006**	Ref	
	Yes	18(29%)	33(53%)		2.78(1.33,5.84)	**0.007**
Length of current marriage in years (Mean ± SD)		8 ± 5.63	8 ± 4.67	0.282	1.01(0.94,1.09)	0.733
Level of education	None	1(2%)	0(0%)	0.263	-	1
	Primary	0(0%)	1(2%)		-	1
	Secondary	3(5%)	7(11%)		2.51(0.62,10.19)	0.199
	Tertiary	58(94%)	54(87%)		Ref	
Occupation	Unemployed	1(2%)	1(2%)	0.661	1.15(0.07,19.07)	0.92
	Self-employed	16(26%)	22(35%)		1.59(0.73,3.44)	0.242
	Employed	45(73%)	39(63%)		Ref	
Smoking	No	62(100%)	60(97%)	0.496	Ref	
	Yes	0(0%)	2(3%)		-	0.999
Alcohol use	No	51(82%)	48(77%)	0.502	Ref	
	Yes	11(18%)	14(23%)		1.35(0.56,3.27)	0.503
BMI	<20	2(3%)	2(3%)	0.909	Ref	
	20- 24.9	20(32%)	16(26%)		0.80(0.10,6.32)	0.832
	25-29.9	19(31%)	20(32%)		1.05(0.13,8.24)	0.961
	>30	21(34%)	24(39%)		1.14(0.15,8.84)	0.898
Depression	No	59(95%)	41(66%)	**<0.001**		
	Yes	3(5%)	21(34%)		10.07(2.82,36.00)	**<0.001**

4.7. Reproductive factors associated with generalized anxiety disorder

Reproductive factors were subjected to a bivariate analysis to establish the association between them and generalized anxiety disorder. The factors that were found to have an association with the symptoms were: primary infertility (p=0.031, OR 0.45, 95%CI 0.22,0.93) and duration of infertility (p=0.052, OR 1.09, 95%CI 1.00,1.19).

With unexplained infertility as the reference, male factor infertility, female factor infertility, and both male and female factor infertility were not associated with generalized anxiety disorder (p=0.84, p=0.194 and p=0.135 respectively). Although patients with a previous history of ART were found to have less odds of having generalized anxiety disorder, it was not statistically significant (p=0.266, AOR 0.66, 95%CI 0.32,1.37). With oral drugs as the reference, ART and surgery were not related to generalized anxiety disorder (p-values 0.585 and 0.799 respectively). Patients with concomitant illnesses in the reproductive tract had greater odds of having generalized anxiety disorder but this was not statistically significant (p=0.082).

Table 8: A table showing the reproductive factors associated with generalized anxiety disorders among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		Anxiety			**Bivariate (unadjusted)**	
		No N=62	**Yes N=62**	**P-value[1]**	**OR (95%CI)**	**P-value[2]**
Previous conception	No	29(47%)	41(66%)	**0.03**	Ref	
	Yes	33(53%)	21(34%)		0.45(0.22,0.93)	**0.031**
Duration of infertility in years (Mean ± SD)		5 ± 4.20	6 ± 4.31	**0.016**	1.09(1.00,1.19)	**0.052**
Cause of infertility	Unexplained	22(35%)	25(40%)	0.114	Ref	
	Male factor	7(11%)	7(11%)		0.88(0.27,2.90)	0.834
	Female factor	30(48%)	20(32%)		0.59(0.26,1.31)	0.194
	Both male and female	3(5%)	10(16%)		2.93(0.72,12.04)	0.135
previous history of ART (IUI/IVF/ICSI)	No	36(58%)	42(68%)	0.265	Ref	
	Yes	26(42%)	20(32%)		0.66(0.32,1.37)	0.266
Type of fertility treatment	Oral drugs	19(31%)	21(34%)	0.746	Ref	
	ART (IUI/IVF/ICSI)	36(58%)	32(52%)		0.80(0.37,1.76)	0.585
	Surgery	7(11%)	9(15%)		1.16(0.36,3.74)	0.799
Concomitant illness in the reproductive tract	No	59(95%)	53(85%)	0.068	Ref	
	Yes	3(5%)	9(15%)		3.34(0.86,12.99)	0.082

4.8. Multivariable regression analysis of factors associated with anxiety

The table below summarizes the results of a logistic regression on the factors affecting anxiety. Previous marriage (p=0.017, AOR 3.02, 95%CI 1.22,7.46), lack of tertiary education (p=6.39, 95%CI 1.38,29.56), duration of infertility (p=0.03, AOR 1.20, 95%CI 1.02,1.42), and depression (p=0.003, AOR 8.35, 95%CI 2.09,33.25) were associated with greater odds of having generalized anxiety disorder after adjusting for all the other sociodemographic and reproductive characteristics.

In the multivariable analysis, generalized anxiety disorder were not found to be associated with the length of current marriage and cause of infertility.

Table 9: A table showing the multivariable regression analysis of factors associated with generalized anxiety disorders among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		AOR (95%CI)	**P-value**
Previous Marriage	No	Ref	
	Yes	2.57(1.08,6.12)	**0.033**
Tertiary level of education	No	6.39(1.38,29.56)	**0.018**
	Yes	Ref	
Length of current marriage in years		0.90(0.79,1.02)	0.108
Duration of infertility in years		1.19(1.02,1.40)	**0.03**
Cause of infertility	Male factor	Ref	
	Female factor	0.59(0.14,2.42)	0.463
	Both male and female	6.47(1.00,41.81)	0.05
	Unexplained	1.35(0.34,5.40)	0.673
Depression	No	Ref	
	Yes	10.25(2.65,39.59)	**0.001**

4.9. Sociodemographic factors associated with depression in patients with infertility

Sociodemographic factors were subjected to a bivariate analysis to establish the association between them and depression. The factors that were found to be significant were: age (p=0.031, OR 1.09, 95%CI 1.01, 1.18) and generalized anxiety disorder (p<0.001, OR 10.07, 95%CI 2.82,36.00). When classified into age groups, none of the groups was found to be statistically significant.

Gender, religion, residence, marital status, previous marriage, length of current marriage, tertiary education, occupation, smoking, alcohol use and BMI had no relationship with depression.

Table 10: A table showing the sociodemographic factors associated with depression among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		Depression			Bivariate (unadjusted)	
		No N= 100	**Yes N=24**	**P-value[1]**	**OR (95%CI)**	**P-value[2]**
Age (Mean ± SD)		37.16 ± 6.068	40.25 ± 6.313	**0.028**	1.09(1.01,1.18)	**0.031**
Age groups	20 - 25	6(6%)	0(0%)	0.343	-	0.999
	26 - 30	6(6%)	2(8%)		0.85(0.15,4.86)	0.854
	31 - 35	27(27%)	4(17%)		0.38(0.11,1.33)	0.129
	36 - 40	33(33%)	7(29%)		0.54(0.19,1.58)	0.26
	>40	28(28%)	11(46%)		Ref	
Gender	Female	83(83%)	20(83%)	0.969	1.02(0.31,3.38)	0.969
	Male	17(17%)	4(17%)		Ref	
Religion	Christian	92(92%)	24(100%)	0.152	-	0.999
	Muslim	8(8%)	0(0%)		Ref	
Residence	Rural	25(25%)	9(38%)	0.218	Ref	
	Urban	75(75%)	15(63%)		0.56(0.22,1.43)	0.221
Marital status	Single	4(4%)	1(4%)	0.729	Ref	
	Married	95(95%)	22(92%)		0.93(0.10,8.70)	0.947
	Divorced/Widowed	1(1%)	1(4%)		4.00(0.12,136.96)	0.442
Previous Marriage	No	62(62%)	11(46%)	0.148	Ref	
	Yes	38(38%)	13(54%)		1.93(0.79,4.74)	0.152
Length of current marriage in years (Mean ± SD)		7.79 ± 4.886	9.23 ± 6.141	0.524	1.05(0.97,1.15)	0.24
Tertiary level of education	No	11(11%)	1(4%)	0.458	Ref	
	Yes	89(89%)	23(96%)		2.84(0.35,23.16)	0.329
Occupation	Unemployed	2(2%)	0(0%)	0.876	-	0.999
	Self-employed	30(30%)	8(33%)		1.13(0.44,2.93)	0.796
	Employed	68(68%)	16(67%)		Ref	
Smoking	No	98(98%)	24(100%)	1	Ref	
	Yes	2(2%)	0(0%)		-	0.999
Alcohol use	No	79(79%)	20(83%)	0.781	Ref	
	Yes	21(21%)	4(17%)		0.75(0.23,2.44)	0.635
BMI	<20	3(3%)	1(4%)	0.634	Ref	
	20- 24.9	31(31%)	5(21%)		0.48(0.04,5.62)	0.562
	25-29.9	29(29%)	10(42%)		1.03(0.10,11.12)	0.978
	>30	37(37%)	8(33%)		0.65(0.06,7.07)	0.722
Anxiety	No	59(59%)	3(13%)	**<0.001**	Ref	
	Yes	41(41%)	21(88%)		10.07(2.82,36.00)	**<0.001**

4.10. Reproductive factors associated with depression

Reproductive factors were subjected to a bivariate analysis to establish the association between them and depression. The factors found to be significant were: duration of infertility (p=0.014, OR 1.13, 95%CI 1.03,1.24) and concomitant illnesses in the reproductive tract (p=0.001, OR 7.82, 95%CI 2.22,27.54).

Most of the patients who were depressed had primary infertility but this was not statistically significant (p=0.119, AOR 2.15, 95%CI 0.82,5.65). Previous history of ART was associated with less odds of having depression but this was also not statistically significant (p=0.073, AOR 0.38, 95%CI 0.13,1.10). Cause of infertility and type of infertility treatment were not associated with depression.

Table 11: A table showing the reproductive factors associated with depression among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		Depression			**Bivariate (unadjusted)**	
		No N= 100	**Yes N= 24**	**P-value[1]**	**OR (95%CI)**	**P-value[2]**
Previous conception	No	53(53%)	17(17%)	0.114	2.15(0.82,5.65)	0.119
	Yes	47(47%)	7(29%)		Ref	
Duration of infertility in years (Mean ± SD)		5.641 ± 3.8862	8.13 ± 5.3816	**0.04**	1.13(1.03,1.24)	**0.014**
Cause of infertility	Unexplained	38(38%)	9(9%)	0.985	Ref	
	Male factor	11(11%)	3(13%)		1.15(0.27,5.00)	0.851
	Female factor	41(41%)	9(38%)		0.93(0.33,2.58)	0.884
	Both male and female	10(10%)	3(13%)		1.27(0.29,5.57)	0.754
Previous history of ART (IUI/IVF/ICSI)	No	59(59%)	19(79%)	0.066	Ref	
	Yes	41(41%)	5(21%)		0.38(0.13,1.10)	0.073
Type of fertility treatment	Oral drugs	31(31%)	9(9%)	0.584	Ref	
	ART (IUI/IVF/ICSI)	57(57%)	11(46%)		0.67(0.25,1.78)	0.416
	Surgery	12(12%)	4(17%)		1.15(0.30,4.44)	0.841
Concomitant illness in the reproductive tract	No	95(95%)	17(71%)	**0.002**	Ref	
	Yes	5(5%)	7(29%)		7.82(2.22,27.54)	**0.001**

4.11 Multivariable analysis of factors associated with depression

The table below shows the results of a logistic regression on the factors associated with depression. Generalized anxiety disorder (p=0.006, AOR 6.57, 95%CI 1.71, 25.24), duration of infertility (p=0.047, AOR 1.13, 95%CI) and concomitant illnesses in the reproductive tract

(p=0.018, AOR 6.12, 95%CI 1.37,27.37) were found to be significantly associated with depression after adjusting for all the other sociodemographic and reproductive characteristics. In the multivariable analysis, depression were not found to be associated with a previous history of ART.

Table 12: A table showing the multivariable regression analysis of factors associated with depression among patients being managed for infertility at two fertility centres in Nairobi between January and March 2022

		AOR (95%CI)	**P-value**
Anxiety	No	Ref	
	Yes	6.57(1.71,25.24)	**0.006**
Duration of infertility in years		1.13(1.00,1.28)	**0.047**
previous history of ART (IUI/IVF/ICSI)	No	Ref	
	Yes	0.30(0.08,1.12)	0.074
Concomitant illness in the reproductive tract	No	Ref	
	Yes	6.12(1.37,27.37)	**0.018**

CHAPTER 5: DISCUSSION

The aim of this study was to establish the prevalence of generalized anxiety disorder and depression as well as their associated factors among patients undergoing treatment for infertility at two fertility centres in Nairobi between January and March 2022. This study, according to our knowledge, is the first one focusing on depressive and generalized anxiety among patients attending fertility centres in Kenya. This enabled us to incorporate patients who were undergoing ART.

According to the results, the prevalence of generalized anxiety disorder was 50%. This is higher than the prevalence of anxiety among the general population in Kenya which stands at 26.3% (11). Among those with these symptoms, 30 had mild anxiety and 20 had severe anxiety. Our findings were similar to a study by Maroufizadeh et al. (49.6%) (20) and almost similar to a study by Joelsson et al. (57.6%) (26). The findings were higher than those found by Yang et al. (7.8%) (27), Yusuf et al. (11.1%) (33), Alosaimi et al. (21.2%) (31), Chen et al. (23.2%) (37), and lower than those found by Yusuf (70%) (28), Abassi et al. (75%) (29) and Ramezanzadeh et al. (86.8%). These differences could be attributed to the use of different tools for assessing the generalized anxiety disorder as well as sociocultural differences due to the different study settings.

This study found a prevalence of 19% for depression. This is higher than the prevalence of depression in the general population in Kenya, 9.3% (11). The prevalence in our study is almost similar to what was found by Yang et al. (20.8%) (27), Yusuf et al. (17.3%) (33), Chen et al. (17%) (37), Alosaimi et al. (21.7%) (31), Joelsson et al. (15.7%) (26). It is lower than that reported by Abbasi et al. (31%) (29), Maroufizadeh et al. (33%) (20), Ramezanzadeh et al. (40.8%) (38) and Yusuf (79%) (28). In addition to the use of different study tools to assess depression, sociocultural differences could explain the differences in the prevalence.

Several factors have been postulated to cause anxiety and depression among patients with infertility. These include the effects of hormonal drugs used in the management of infertility, the cost of treatment, uncertainty about the treatment outcomes and societal pressure (18,20).

In this study, the factors found to be associated with generalized anxiety disorder were previous marriage, duration of infertility, lack of tertiary education and co-existing depression. This study found that factors associated with depression were the duration of infertility, concomitant illnesses in the reproductive tract and co-existing generalized anxiety disorder.

The findings of an association between the duration of infertility and generalized anxiety disorder in this study are similar to studies by Yang et al. (27) and Ramezanzadeh et al. (38).

The longer a couple has had infertility, the more likely they are to have tried different treatment options. This involves investing emotionally, spiritually and financially and can explain why such patients are likely to experience anxiety and depression especially when the treatment fails. Previous marriage as a factor can be explained by the fear of the marriage coming to an end especially if infertility was responsible for the divorce.

Unlike this study which found a relationship between lack of tertiary education and generalized anxiety disorder, studies by Yang et al. (27) and Yusuf (28) found no relationship between the two. Most participants in the study by Yang et al. had only attained secondary education while 90% of the participants in this study had tertiary education. The fact that a minority of the participants in this study (10%) lacked tertiary education makes it difficult to generalize this to our population.

Similar to the findings in this study, studies by Yang et al. (27) and Abass et al. (32) found an association between the duration of infertility and depression. The longer a couple has had infertility, the more likely they are to have experienced societal pressure, stigma and low self-esteem. They are also likely to have tried different treatment options including herbs and supplements without any success. Infertility has also been found to have a negative impact on marital relationships (48–50) and this could predispose individuals to depression.

There was a relationship between concomitant illnesses in the reproductive tract and depression in this study. This is similar to a study by Yang et al. (27). Some patients with infertility have other illnesses in the reproductive tract which have been reported to affect fertility. These include varicocele, erectile dysfunction, ejaculatory disorders and vaginismus. Vaginismus is associated with involuntary vaginal spasms which impair penetration hence leading to infertility (51). Erectile dysfunction and ejaculatory disorders can either be a direct cause or consequence of infertility (52). Though controversial, varicocele has been associated with male infertility (53). These conditions affect sexual function and have a negative impact on one's self esteem, marriage, sexual satisfaction and quality of life which can lead to depression. This explains our finding of an association between concomitant illnesses in the reproductive tract and depression.

Some of these conditions affect sexual function and have a negative impact on an individual's quality of life and this could explain why they are associated with symptoms of depression.

Findings from this study show that depression and anxiety have a bidirectional relationship. Generalized anxiety disorder were found to be associated with depression and vice versa. This is in line with a meta- analysis done by Jacobson and Newman (54) which found a relationship between the two conditions.

ART was not found to be associated with symptoms of either generalized anxiety disorder or depression in this study. This is contrary to a study by Lakatos et al. (25) which revealed that ART was associated with depression but not anxiety. This could be attributed to the fact that the study by Lakatos et al. was conducted in a high income country where ART is done more commonly than in our setting. A previous history of ART was also not found to be associated with symptoms of either condition.

The most common cause of infertility in this study was female factor infertility at 40%. Combined male and female factor infertility was the least common cause of infertility at 10%. This is different from what has been found in other regions (3). This could be attributed to the fact that most participants in our study were female because fewer men present to health facilities for management of infertility in Kenya. None of the causes of infertility was associated with generalized anxiety disorder or depression in this study. This could also be explained by the fact that most patients were female hence making it difficult to get an association.

Most participants in this study had primary infertility (56%). Primary infertility was not found to be associated with generalized anxiety disorder or depression. This is contrary to a study by Abass et al. (32) which found an association between primary infertility and depression. This could be due to the differences in the prevalence of primary infertility in the two studies since the one by Abass et al. had a prevalence of 38%.

In conclusion, it is clear from the findings of this study that individuals affected by infertility suffer from generalized anxiety disorder and depression. Factors associated with generalized anxiety disorder were found to be previous marriage, duration of infertility, lack of tertiary education and co-existing depression while those associated with depression were duration of infertility, concomitant illnesses in the reproductive tract and co-existing anxiety. We recommend the incorporation of psychological support in the routine management of infertility as well as holistic care, including referral to fertility specialists, for patients being managed for anxiety and depression with underlying infertility.

5.1. Conclusion

Patients undergoing treatment for infertility in our setting are affected by anxiety and depression. The factors found to be associated with symptoms of the former were: previous marriage, duration of infertility, lack of tertiary education and co-existing depression. Factors associated with the latter were: duration of infertility, concomitant illnesses in the reproductive tract and co-existing anxiety.

5.2. Recommendations

Based on our findings, we recommend that psychological support should be offered to couples undergoing treatment for infertility as part of routine care. Since infertility has been found to be associated with depression and anxiety, we recommend that psychiatrists and psychologists should probe patients found to have either condition for their family history in order to establish whether infertility could be a factor and refer them for holistic care.

5.3. Strengths and limitations

Strengths

i. The focus of the study was on symptoms of both depression and generalized anxiety disorder, the predominant psychiatric disorders among infertile individuals.
ii. The use of standardized scales (BDI and STAI) which have been used in similar studies to assess for depressive symptoms as well as generalized anxiety disorder, respectively, improved both the reliability and validity of data collected.
iii. Conducting the study in fertility centres that have access to ART in Kenya made this study original in the local context

Limitations

It was difficult to establish a cause-and-effect relationship between the variables since it is a cross-sectional study. A multivariable analysis was done to establish an association between the variables.

5.4. The study budget

Table 13: A table showing the study budget

Items	**Cost**	**Unit**	**Total (KSH)**
KNH-UON ERC submission (a)	2000	1	**2,000**
STATIONERY (b)			
Data collection tool printing	16 pages * Ksh. 10/page	130	20,880
Thesis printing	100 pages * Ksh. 10/ page	10	10,000
Sub-Total			**30,880**
WAGES (c)			
Research Assistants (RAs)			51,000
Data Analysts		1	30,000
Sub-Total			**81,000**
EXPENSES (d)			
Communication			2,000
Publication			15,000
Sub-Total			**17,000**
Contingencies (e)	15% of total budget (a, b, c, d)		**19,632**
TOTAL	**(a+b+c+d+e)**		**150,512**

Budget justification

The budget items were priced according to the market rates at the time.

1. KNH-UON Ethical review cost KSH. 2,000 per manuscript.
2. The cost of printing was estimated to be KSH. 10 per page.
3. Research assistants were reimbursed at an agreed upon rate of KSH. 51,000 in total.
4. A statistician was reimbursed as per market rate to a total of KSH. 30,000 for data analysis.
5. Communication with research assistants including internet bundles for research cost KSH. 2,000
6. A 15% contingency fee was factored in the research in case of other emerging unforeseen expenses.

5.5. Study timelines

Table 14: A table showing the study work plan

	Jan 2021 - June 2021	July 2021- December 2021	January 2022- March 2022	April 2022	May 2022
PROPOSAL DEVELOPMENT					
ETHICAL CLEARANCE					
DATA COLLECTION					
DATA ANALYSIS & REPORT WRITING					
PRESENTATION / PUBLICATION					

REFERENCES

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CHAPTER 6: APPENDICES

6.1. Appendix I: Consent form

English version

Title: ANXIETY AND DEPRESSION AMONG PATIENTS TREATED AT TWO FERTILITY CENTRES IN NAIROBI; PREVALENCE AND ASSOCIATED FACTORS: A DESCRIPTIVE CROSS-SECTIONAL STUDY

Background

Infertility negatively affects one's self-esteem, identity, goals, and relationships. While previous studies described psychological distress as a cause of infertility, more recent studies have shown that infertility can result in psychological distress. This study aims to evaluate the prevalence and associated factors of depressive and anxiety in patients being managed for infertility in two fertility centres in Nairobi.

Principal investigator and reason for conducting the study

I am Dr. Joy Kalondu Ngoloma, the principal investigator in this study. I am a postgraduate student at the Department of Obstetrics and Gynaecology, University of Nairobi. I am conducting this study because I would like to highlight the psychological effects of infertility among patients undergoing fertility treatment and establish the factors that are associated with psychological effects. In so doing, my intention is to justify the need for incorporating mental health support as part of routine management for infertility.

Why are you invited to participate in this study?

You are invited to participate in this study to help highlight the need for mental health support in the management of infertility. The information you will provide in the attached questionnaire could help inform policy on the management of infertility in Kenya.

Methods and procedures

The same questionnaire will be administered to men and women being managed for infertility in two fertility centres in Nairobi.

Risks and benefits

Agreeing to participate in this study is likely to be associated with a risk of invasion of privacy due to the nature of items included in the self-assessment scales for depression and generalized anxiety disorder. In addition to this, some of the questions may elicit discomfort and emotional distress. However, this will be mitigated by observing confidentiality. Information obtained from you, the participant, will not be shared outside this study. Your personal information (e.g., name, address) will not be included in the questionnaire hence there is no risk of personally identifying any respondent in the analyzed results.

Screening for depression and generalized anxiety disorder will be done at no extra cost to you. Should you be found to have depression and/or generalized anxiety disorder, you will be referred to the Department of Mental Health, Kenyatta National Hospital, for treatment and follow up.

Right not to participate and withdraw

Your participation in this study is completely voluntary, and you have the sole authority to withdraw at any point. Failure to take part in this study or withdrawing from the study will not affect the quality of care you will receive at the fertility centre.

Principle of compensation

You will not be paid for agreeing to be part of this study.

Contact persons

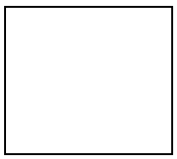
You may contact Dr. Joy Ngoloma on 0721 575776 should any questions or concerns on this study arise.

Should you have any concerns about this study, you are also free to contact the Kenyatta National Hospital/University of Nairobi Ethics Research Committee (KNH-UoN ERC) via uonknh_erc@uonbi.ac.ke.

If you agree to participate in this study, please indicate that by putting your signature or your left thumb print at the specified space below.

Thank you for your cooperation

_____	_____	_____
Name of the Interviewer	Signature of the Interviewer	Date



If the participant is illiterate/unable to write in that case please take her/his left thumb impression

_____	_____	_____
Code	Signature of the Respondent	Date

Kiswahili version

Fomu ya Idhini:

Kichwa: ANXIETY AND DEPRESSION AMONG PATIENTS TREATED AT TWO FERTILITY CENTRES IN NAIROBI; PREVALENCE AND ASSOCIATED FACTORS: A DESCRIPTIVE CROSS-SECTIONAL STUDY

Historia

Hali ya utasa huadhiri heshima, utambulisho, malengo pamoja na mahusiano katika maisha ya wagonjwa walioadhirika. Utafiti wa hapo awali ulionyesha kwamba magonjwa ya kiakili yalikuwa yakisababisha hali ya utasa lakini utafiti wa hivi karibuni unadhihirisha kwamba hali ya utasa huweza kusababisha magonjwa ya kiakili. Utafiti huu unatarajia kuchunguza uwepo wa unyogovu wa akili pamoja na ugonjwa wa wasiwasi miongoni mwa watu wanaotibiwa hali ya utasa katika vituo viwili vya matibabu ya utasa jijini Nairobi.

Kwa nini umealikwa kushiriki katika utafiti?

Kushiriki kwako katika utafiti huu kutadhihirisha umuhimu wa masuala ya magonjwa ya kiakili katika matibabu ya hali ya utasa. Taarifa itakayotokana na utafiti huu inaweza kutumika kubuni sera za matibabu ya hali ya utasa nchini Kenya.

Njia na taratibu

Orodha ya maswali ya uchunguzi itatumika kwa wanwake na wanaume wanaotibiwa hali ya utasa katika vituo viwili vya matibabu ya utasa jijini Nairobi.

Matatizo na Manufaa

Kuna uwezekano wa kuathirikia kihisia kutokana na kujihusisha katika utafiti huu.Taarifa itakayopatikana kutoka kwako kama mshiriki haitashirikiwa nje ya utafiti huu. Maelezo yako ya kibinafsi (kama vile jina na anwani) hayataandikwa kwenye orodha ya maswali ya uchunguzi kwa hivyo hakutakuwa na hatari ya kutambua kibinafsi mtu yeyote katika matokeo yetu kuchambuliwa. Hutakuwa na faida yoyote ya moja kwa moja kwa kushiriki katika utafiti huu.

Haki ya kushiriki na kujiondoa

Ushiriki wako katika utafiti huu ni kwa hiari, na una mamlaka pekee ya kuamua au dhidi ya ushiriki wako katika utafiti huu. Kutoshiriki au kujiondoa kutoka kwa utafiti huu hautaathiri matibabu utakayopokea katika kituo hiki.

Kanuni ya fidia

Hatutakulipa kwa kukubali kushiriki katika utafiti huu.

Kujibu maswali yako / mawasiliano

Unaweza kuwasiliana na Dr. Joy Ngoloma kwa namba ya simu 0721 575 776 kuhusu maswali uliyo nayo kuhusu utafiti huu.Ikiwa unakubaliana na pendekezo lako la kujiandikisha katika masomo yetu, tafadhali onyesha hivyo kwa kuweka saini yako au alama ya kidole chako cha kushoto katika nafasi maalum. Vilevile, iwapo na maswali zaidi, unaweza kutuma barua pepe kwenye anwani hii ya KNH-UoN ERC: uonknh_erc@uonbi.ac.ke.

Asante kwa ushirikiano wako.

_____	_____	_____
Jina la Mhojiwa	Sahihi ya Msaidizi	Tarehe

	Ikiwa mshiriki hajui kusoma / hawezi kuandika, katika kesi hiyo tafadhali piga picha kidole ya kushoto

_____	_____	_____
Jina la Mhojiwa	Sahihi ya Msaidizi	Tarehe

6.2. Appendix II: Questionnaire

ANXIETY AND DEPRESSION AMONG PATIENTS TREATED AT TWO FERTILITY CENTRES IN NAIROBI; PREVALENCE AND ASSOCIATED FACTORS: A DESCRIPTIVE CROSS-SECTIONAL STUDY

Section 1: Sociodemographic and reproductive characteristics

1. Age _____ years
2. Sex:

   Male ☐ Female ☐
3. Religion:

   Christian ☐ Muslim ☐ Hindu ☐

4. Residence:

   Urban ☐ Rural ☐
5. Marital status:

   Single ☐ Married ☐ Divorced/Widowed ☐

6. If married:

   Number of previous marriages (if applicable):

   1 ☐ 3 ☐

   2 ☐ Other ☐

   If other, explain _____

   Length of current marriage: _____ years
7. Level of education:

   None ☐ Secondary ☐

   Primary ☐ Tertiary (college/university) ☐
8. Occupation:

   Unemployed ☐ Self-employed ☐ Employed ☐
9. Smoking:

   Yes ☐ No ☐
10. Alcohol use:

Yes ☐ No ☐

11. Weight: _____ kg

12. Height: _____ metres

13. Previous conception:

Yes ☐ No ☐

14. Duration of infertility: _____ years

15. Cause of infertility:

Female factor ☐

Male factor ☐

Both male and female ☐

Unexplained ☐

16. Previous history of ART (IUI/IVF/ICSI):

Yes ☐ No ☐

17. Number of previous ART: _____

18. Type of fertility treatment:

Oral drugs ☐

Surgery ☐

ART (IUI/IVF/ICSI) ☐

19. Concomitant illness in the reproductive tract:

If male:

None ☐

Varicocele ☐

Erectile dysfunction ☐

Ejaculatory dysfunction ☐

If female:

None ☐

Vaginismus ☐

Pain during sexual intercourse (dyspareunia) ☐

Section 2: Beck Depression Inventory

This section contains 21 multiple choice items. Please tick the box that most appropriately

describes your current state.

1. ☐ 0 I do not feel sad.
   ☐ 1 I feel sad.
   ☐ 2 I am sad all the time and I can't snap out of it.
   ☐ 3 I am so sad and unhappy that I can't stand it.

2. ☐ 0 I am not particularly discouraged about the future.
   ☐ 1 I feel discouraged about the future.
   ☐ 2 I feel I have nothing to look forward to.
   ☐ 3 I feel the future is hopeless and that things cannot improve.

3. ☐ 0 I do not feel like a failure.
   ☐ 1 I feel I have failed more than the average person.
   ☐ 2 As I look back on my life, all I can see is a lot of failures.
   ☐ 3 I feel I am a complete failure as a person.

4. ☐ 0 I get as much satisfaction out of things as I used to.
   ☐ 1 I don't enjoy things the way I used to.
   ☐ 2 I don't get real satisfaction out of anything anymore.
   ☐ 3 I am dissatisfied or bored with everything.

5. ☐ 0 I don't feel particularly guilty.
   ☐ 1 I feel guilty a good part of the time.
   ☐ 2 I feel quite guilty most of the time.
   ☐ 3 I feel guilty all of the time.

6. ☐ 0 I don't feel I am being punished.

☐ 1 I feel I may be punished.

☐ 2 I expect to be punished.

☐ 3 I feel I am being punished.

7. ☐ 0 I don't feel disappointed in myself.

☐ 1 I am disappointed in myself.

☐ 2 I am disgusted with myself.

☐ 3 I hate myself.

8. ☐ 0 I don't feel I am any worse than anybody else.

☐ 1 I am critical of myself for my weaknesses or mistakes.

☐ 2 I blame myself all the time for my faults.

☐ 3 I blame myself for everything bad that happens.

9. ☐ 0 I don't have any thoughts of killing myself.

☐ 1 I have thoughts of killing myself, but I would not carry them out.

☐ 2 I would like to kill myself.

☐ 3 I would kill myself if I had the chance.

10. ☐ 0 I don't cry any more than usual.

☐ 1 I cry more now than I used to.

☐ 2 I cry all the time now.

☐ 3 I used to be able to cry, but now I can't cry even though I want to.

11. ☐ 0 I am no more irritated by things than I ever was.

☐ 1 I am slightly more irritated now than usual.

☐ 2 I am quite annoyed or irritated a good deal of the time.

☐ 3 I feel irritated all the time.

12. ☐ 0 I have not lost interest in other people.

☐ 1 I am less interested in other people than I used to be.

☐ 2 I have lost most of my interest in other people.

☐ 3 I have lost all of my interest in other people.

13. ☐ 0 I make decisions about as well as I ever could.

☐ 1 I put off making decisions more than I used to.

☐ 2 I have greater difficulty in making decisions more than I used to.

☐ 3 I can't make decisions at all anymore.

14. ☐ 0 I don't feel that I look any worse than I used to.

☐ 1 I am worried that I am looking old or unattractive.

☐ 2 I feel there are permanent changes in my appearance that make me look unattractive.

☐ 3 I believe that I look ugly.

15. ☐ 0 I can work about as well as before.

☐ 1 It takes an extra effort to get started at doing something.

☐ 2 I have to push myself very hard to do anything.

☐ 3 I can't do any work at all.

16. ☐ 0 I can sleep as well as usual.

☐ 1 I don't sleep as well as I used to.

☐ 2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.

☐ 3 I wake up several hours earlier than I used to and cannot get back to sleep.

17. ☐ 0 I don't get more tired than usual.

☐ 1 I get tired more easily than I used to.

☐ 2 I get tired from doing almost anything.

☐ 3 I am too tired to do anything.

18. ☐ 0 My appetite is no worse than usual.

☐ 1 My appetite is not as good as it used to be.

☐ 2 My appetite is much worse now.

☐ 3 I have no appetite at all anymore.

19. ☐ 0 I haven't lost much weight, if any, lately.

☐ 1 I have lost more than 2kg.

☐ 2 I have lost more than 5kg.

☐ 3 I have lost more than 7kg.

20. ☐ 0 I am no more worried about my health than usual.

☐ 1 I am worried about physical problems like aches, pains, upset stomach, or constipation.

☐ 2 I am very worried about physical problems and it's hard to think of much else.

☐ 3 I am so worried about my physical problems that I cannot think of anything else.

21. ☐ 0 I have not noticed any recent change in my interest in sex.

☐ 1 I am less interested in sex than I used to be.

☐ 2 I have almost no interest in sex.

☐ 3 I have lost interest in sex completely.

Section 3: State-Trait Anxiety Inventory

This section contains 20 multiple choice items. Please tick the option that most appropriately represents how you currently feel.

	1 (Not at all)	2 (A little)	3 (Somewhat)	4 (Very much so)
I feel calm.				
I feel secure.				
I feel tense.				
I feel strained.				
I feel at ease.				
I feel upset.				
I am presently worrying over possible misfortunes.				
I feel satisfied.				
I feel frightened.				
I feel uncomfortable.				
I feel self-confident.				
I feel nervous.				
I feel jittery.				
I feel indecisive.				
I am relaxed.				
I feel content.				
I am worried.				
I feel confused.				
I feel steady.				
I feel pleasant.				

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Ref: KNH-ERC/A/469

9th December 2021

Dr. Joy Kalondu Ngoloma
Reg. No.H58/34241/2019
Dept. of Obstetrics and Gynaecology
Faculty of Health Sciences
University of Nairobi

Dear Dr. Ngoloma

RESEARCH PROPOSAL: ANXIETY AND DEPRESSION AMONG PATIENTS TREATED AT TWO FERTILITY CENTRES IN NAIROBI; PREVALENCE AND ASSOCIATED FACTORS: A DESCRIPTIVE CROSS-SECTIONAL STUDY (P795/10/2021)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P795/10/2021.** The approval period is 9th December 2021 – 8th December 2022.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely

PROF. M.L. CHINDIA
SECRETARY, KNH-UON ERC

c.c. The Dean-Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Chair, Dept. of Obstetrics and Gynaecology, UoN
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