Prevalence and severity of depression and anxiety in infertile female patients attending an academic hospital in central South Africa

T Mulondo,[1] MB ChB; **S Baloyi,**[1,2] MB ChB, MMed,; **J B Sempa,**[3] PhD

[1]*Department of Obstetrics and Gynaecology, School of Clinical Medicine, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*
[2]*School of Medicine, Faculty of Health Sciences, University of Limpopo, Polokwane, South Africa*
[3]*Department of Biostatistics, School of Biomedical Sciences, Faculty of Health Sciences, University of the Free State, Bloemfontein, South Africa*

Corresponding author: *T Mulondo (takalani.mulondo@gmail.com)*

Background. Infertility has an incidence of 15 - 20% in South Africa (SA). It may lead to the development of psychological disorders such as anxiety and depression.
Objective. To determine the prevalence of depression and anxiety among infertile women attending the Infertility Clinic at a tertiary hospital in central SA.
Methods. In this prospective analytic cross-sectional study, information captured included sociodemographic variables such as age, employment status, type and duration of infertility, marital status, type of marriage and education level. The Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder-7 (GAD-7) test were used to screen for depression and anxiety, respectively.
Results. In total, 100 of 108 infertile women completed all the questionnaires correctly. Forty-two (42.0%) of the patients were >35 years and 58.0% were married, with five (8.6%) being in a polygamous marriage. Fifty-three (53.0%) women had never been pregnant before. The prevalence of depression was 53.0%, with 45.0% of these patients showing moderate to moderately severe levels of depression. The level of education was significantly associated with depression ($p<0.025$). Half of the participants (50.0%) screened positive for anxiety, with 12 (24.0%) having severe anxiety. In total, 40.0% of the participants screened positive for both anxiety and depression. No statistically significant association was observed between depression or anxiety and age, duration of infertility, marital status and employment status.
Conclusions. Depression and anxiety disorders are common and often underdiagnosed in women undergoing infertility treatment. Practitioners should screen for these conditions at the initial patient presentation and refer patients for psychological support.
Keywords. Depression, anxiety, infertility, women, prevalence.

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Infertility is defined as a failure to achieve a clinical pregnancy after 12 months or more of regular, unprotected sexual activity, indicating a disorder of the reproductive system.[1] Infertility often leads to feelings of defectiveness regarding the role of motherhood or a loss of true femininity, which can be extremely upsetting for infertile women.[2] Children fulfil a need for family stabilisation and are highly valued members of society. They can be a form of social security in their parents' old age, perpetuating the family lineage and increasing marital satisfaction.[2] Severe adverse reactions related to infertility include sadness, denial, melancholy, anxiousness, guilt, loss of control, self-blame, challenges to one's self-esteem, marital misery, sexual dysfunction and issues in interpersonal connections, such as emotions of rage towards child-parenting couples. These adverse reactions could lead to depression and anxiety.[3]

Depression is a common mental disorder and patients can manifest in a variety of ways, including exhibiting symptoms such as anxiety, powerlessness, lack of motivation or sexual desire, sleep and eating disturbances and suicidal thoughts.[4] The World Health Organization (WHO) regards depression as a common cause of disability worldwide,[1] with the potential to surpass both heart disease and cancer as a cause of disability.[5] Predictive factors of anxiety and depression in infertile couples include previous marriage, being female, being in a polygamous relationship, having a lower education level, lacking support, being subject to stigmatising behaviour, having received surgical treatment of infertility, a long duration of infertility and repeated treatment cycles.[2-7] Infertile women are also more likely to have anxiety symptoms than infertile men,[8] prompting the importance of paying attention to the mental health of women undergoing infertility treatment. In the early stages of infertility, couples are hopeful about the possible results with medical intervention, and they receive support from their physicians and relatives in striving to increase the possibility of pregnancy.[9] A long duration of infertility and repeated referrals to physicians are serious physical stress factors for infertile individuals and are accompanied by anxiety about the effectiveness of medical intervention. Infertility-causing hormonal abnormalities may also increase a person's susceptibility to depressive symptoms and mood disorders.[4]

It is important to screen for depression and anxiety because women who test positive for depression are more likely to put off starting fertility treatment and are less likely to seek treatment with oral medication or in vitro fertilisation.[5] Infertility could gradually change into a chronic problem owing to the inability to achieve one of the most important goals of marriage, which is to reproduce.[9] It is crucial to evaluate the mental wellbeing of these patients during their

infertility follow-ups because of the high rate of infertility and the increasing number of couples seeking treatment for infertility.[3]

The aim of this study was to screen for the presence and severity of depression and anxiety and associated factors in infertile women attending the Infertility Clinic at Universitas Academic Hospital (UAH), a tertiary public hospital in Bloemfontein, SA.

Methods

Study design and setting

A prospective cross-sectional study design was applied. This research was conducted at the Infertility Clinic of UAH, the largest tertiary public healthcare institution in the Free State Province of SA. The study aimed to comply with the United Nations (UN) Sustainable Development Goal 3: Good Health and Well-being.

Study population and sampling strategy

Convenience sampling was used, and 108 women who met the inclusion criteria consented to participate in the study. Data were collected from January 2021 - February 2022.

The inclusion criteria were as follows: (1) be ≥18 years of age, (2) be able to complete a questionnaire, (3) consent to participate in the research and (4) have no history of mental illness. Patients with a prior documented diagnosis of psychiatric illness reported in their medical records were excluded from the study.

Measurements

Three instruments; an individual sociodemographic questionnaire, the Patient Health Questionnaire comprising nine items (PHQ-9) and the Generalized Anxiety Disorder test comprising seven items (GAD-7), were used to obtain information.

Individual sociodemographic questionnaire

This instrument collected data pertaining to the participants' age, employment status, type of infertility (primary infertility – had never been pregnant before; secondary infertility – had been pregnant before), duration of infertility, marital status, type of marriage (monogamous; polygamous) and level of education.

Patient Health Questionnaire-9

This nine-item pretested and validated self-report instrument was used to screen for depression.[10] The PHQ-9 is also generally used for monitoring patients' responses to depression treatment. Scores from 0 - 27 can be obtained, with scores ≥10 indicating a possible major depressive disorder. It also includes a question that assesses whether depressive symptoms impair social functioning, which is one of the key criteria to establish a Diagnostic and Statistical Manual of Mental Disorders (DSM)-based diagnosis of depression. A PHQ-9 score of 10 or higher has 88% sensitivity and 88% specificity to detect major depressive disorder. A score less than 10 yields a negative predictive value of 99%. PHQ-9 score cut-offs grade the severity of the depressive symptoms experienced: scores of 0 - 4 indicate the absence of depression, 5 - 9 represent mild depression, 10 - 14 moderate depression, 15 - 19 moderately severe depression and a score ≥20 indicates severe depression.[10]

Generalized Anxiety Disorder seven-item scale

The GAD-7 is used to screen for symptoms of generalised anxiety disorder.[11] It has acceptable reliability and criterion, construct, factorial and procedural validity. The GAD-7 provides a possible score from 0 to 21, and a score equal to or greater than 10 has 89% sensitivity and 82% specificity to detect the presence of generalised anxiety disorder that warrants further assessment. In our study, we used the proposed cut-off value of ≥10 to identify participants with possible generalised anxiety disorder. The scoring levels of GAD-7 reflect the severity of anxiety symptoms: a score of 0 - 4 represents minimal anxiety, 5 - 9 mild anxiety, 10 - 14 moderate anxiety and 15 - 21 severe anxiety.[11]

Procedure

All women who met the criteria for inclusion in the study were recruited on the days of data collection. Informed consent was obtained before the participants were handed the data collection tools for completion with the assistance of the investigator. After the assessment of the questionnaires, all research participants who tested positive for either anxiety or depression were counselled on the findings of the research and were then referred for further psychological assessment and management by a mental health practitioner.

Data analysis

Collected data were entered into a Microsoft Excel version 2016 spreadsheet and submitted to the Department of Biostatistics, Faculty of Health Sciences, University of the Free State, for statistical analysis using R, version 4.2.2 (R Foundation for Statistical Computing, Austria). Results were summarised by frequencies and percentages for categorical variables and means or medians and percentiles for numerical variables. For variable comparisons with depression and anxiety, $p<0.05$ was considered statistically significant.

Ethical considerations

The research protocol was approved by the Health Science Research Ethics Committee (HSREC) of the University of the Free State (ref. no. UFS-HSD2020/0721/2909). Permission to conduct the study was obtained from the Free State Province Department of Health. The head of the Department of Obstetrics and Gynaecology, UAH, was permitted to conduct the study at the Infertility Clinic. All recruited participants were informed on the nature of the research and written consent was obtained from each participant before the commencement of data collection. These consent forms were made available in the three local languages, Sesotho, English and Afrikaans. All completed questionnaires were collected and handled only by the primary investigator (TM) to ensure confidentiality.

Results

Sociodemographic characteristics

During the study period, 108 women who met the inclusion criteria consented to participate in the study. They all completed the three questionnaires. One hundred participants completed all the questionnaires correctly and these questionnaires were included in the statistical analysis of data. More than half (n=53; 53.0%) of the participants were aged between 25 and 34 years, while 42 (42.0%) participants were older than 35 years (Table 1). Five participants did not provide information on their age.

As shown in Table 1, approximately two-thirds of the women had been suffering from infertility for a period ranging between 1 and 5 years (61.0%), with the least number of participants (16.0%) reporting infertility lasting more than 10 years. Regarding the latter group, it was not ascertained how long it took before they attended infertility services. Slightly more than half of the participants (53.0%) were women who were suffering from primary infertility. In total, 58.0% of the participants were married, of whom five (8.6%) reported being in polygamous marriages. Of the 100 participants, 63.0% had

completed schooling up to Grades 8 - 12, while only two (2.0%) received no formal education. Approximately half (51.0%) of the respondents were unemployed.

Prevalence and severity of depression and anxiety

Of the 100 respondents in the study, 53.0% screened positive for a diagnosis of depression (PHQ-9 score ≥10) (Table 2). In total, 51.0% of the participants had mild to moderate depressive symptoms, whereas 8.0% obtained scores (≥20) indicative of severe depression. Of 53 patients, 28 (52.8%) described their depression symptoms as making their life somewhat difficult to perform daily household duties or interact with other people.

Half the patients (50.0%) screened positive for a diagnosis of moderate to severe anxiety disorder (GAD-7 score ≥10). Approximately one-quarter of these 50 women (*n*=12; 24.0%) had scores representing a severe level of anxiety and a further 26.0% (*n*=13) of women had a moderate level of anxiety (Table 2). Some women (*n*=12/50; 24.0%) who screened positive for generalised anxiety disorder reported that their anxiety symptoms made their lives extremely difficult, affecting their ability to perform daily tasks and negatively impacting their social relationships. Twenty-three (46.0%) reported their lives were somewhat difficult, and six women reported that those anxiety symptoms had not made their lives difficult at all. In total, 40.0% of the study population screened positive for both depression and generalised anxiety disorder.

Table 1. Sociodemographic characteristics of study participants (*N*=100 for all demographic variables, unless specified otherwise)

Variable	*n* (%)
Age (years)	
18 - 24	5 (5.0)
25 - 34	53 (53.0)
>35	42 (42.0)
Duration of infertility (years)	
1 - 5	61 (61.0)
6 - 10	23 (23.0)
>10	16 (16.0)
Marital status	
Single	19 (19.0)
Married	58 (58.0)
Widowed	2 (2.0)
Divorced	1 (1.0)
Engaged	20 (20.0)
Type of marriage (*n*=58)	
Monogamous	53 (91.4)
Polygamous	5 (8.6)
Level of education	
None	2 (2.0)
Grades 1 - 7	6 (6.0)
Grades 8 - 12	63 (63.0)
Tertiary level	29 (29.0)
Employment	
Unemployed	51 (51.0)
Self-employed	8 (8.0)
Employed	41 (41.0)
Type of infertility*	
Primary	53 (53.0)
Secondary	47 (47.0)

*Primary – had never been pregnant; secondary – had been pregnant before.

Sociodemographic factors associated with depression

Table 3 depicts the sociodemographic factors associated with depression among the women who attended the Infertility Clinic. Of the participants who screened positive for depression (*n*=53), most were aged 25 - 34 years (*n*=34; 64.2%). They had been suffering from infertility for 1 - 5 years (*n*=33; 62.3%), were married (*n*=28; 52.8%), had been pregnant before (*n*=29; 54.7%), were unemployed (*n*=29; 54.7%) and had a level of education ranging between at least Grade 8 and a tertiary qualification (*n*=45; 84.9%). The level of education showed a significant association with depression ($p<0.025$).

PHQ-9 severity by sociodemographic factors

Supplementary Table 1 (https://www.samedical.org/file/2244) summarises the PHQ-9 severity level by sociodemographic factors. Approximately half (*n*=27; 50.9%) of the participants who screened positive for depression presented with a moderate level of depression. Of the 34 women aged 25 - 34 years who screened positive for depression, 30 (88.2%) had moderate to moderately severe levels of depression features, while eight (23.5%) participants in this age group presented with severe depressive symptoms. Of the women who reported suffering from infertility for a duration of 1 - 5 years (*n*=33), 29 (87.8%) also presented with moderate to moderately severe depression. In total,

Table 2. Prevalence and severity of depression and anxiety (*N*=100 for all demographic variables, unless specified otherwise)

Variable	*n* (%)
Patient Health Questionnaire (PHQ-9) score	
≥10	53 (53.0)
<10	47 (47.0)
Depression severity (score)	
Absent (0 - 4)	23 (23.0)
Mild (5 - 9)	24 (24.0)
Moderate (10 - 14)	27 (27.0)
Moderately severe (15 - 19)	18 (18.0)
Severe (≥20)	8 (8.0)
Difficulty level of depression (*n*=53)	
Not difficult	7 (13.2)
Somewhat difficult	28 (52.8)
Very difficult	14 (26.4)
Extremely	4 (7.5)
Generalized Anxiety Disorder (GAD-7) score	
<10	50 (50.0)
≥10	50 (50.0)
Anxiety severity (score)	
Minimal (0 - 4)	22 (22.0)
Mild (5 - 9)	28 (28.0)
Moderate (10 - 14)	26 (26.0)
Severe (15 - 21)	24 (24.0)
Difficulty level of anxiety (*n*=50)	
Not difficult	6 (12.0)
Somewhat difficult	23 (46.0)
Very difficult	15 (30.0)
Extremely difficult	6 (12.0)
Both anxiety depression	40 (40.0)

12 of the 28 (42.9%) depressed married women had moderate levels of depression, while 27 of the 53 (50.9%) women with either primary or secondary infertility had moderate levels of depression, with four women in each category (*n*=4/29; 13.8% and *n*=4/24; 16.7%, respectively) presenting with severe depressive symptoms. No statistically significant association was found between the severity of depression and any of the sociodemographic factors investigated.

GAD-7 scores

Supplementary Table 2 (https://www.samedical.org/file/2244) shows the participants' GAD-7 scores. Of the 50 women who screened positive for anxiety (score ≥10), 29 (58.0%) women were 25 - 34 years of age, with only one participant aged 18 - 24 years having anxiety disorder. Thirty (60.0%) of the women with anxiety had been suffering from infertility for 1 - 5 years, 28 (56.0%) were married and 45 (90.0%) had a level of education of Grade 8 or higher. No significant association was found between GAD-7 and any of the sociodemographic factors that were investigated.

Sociodemographic factors associated with GAD-7 and severity levels

Supplementary Table 3 (https://www.samedical.org/file/2244)represents the association between the different levels of anxiety and sociodemographic factors. Slightly more than a quarter (26.0%) of the participants presented with moderate levels of anxiety. In total, 24% of the participants were identified with severe levels of anxiety. Thirteen (54.2%) of the 24 women with severe anxiety were aged between 25 and 34 years, 15 (62.5%) had been suffering from infertility for 1 - 5 years, 11 (45.8%) were married, 21 (87.5%) had a level of education of at least Grade 8 - 12, 14 (58.3%) were unemployed and 14 (58.3%) were suffering from secondary infertility.

Association between GAD-7 and PHQ-9 scores by social demographics

A total of 40 study participants screened positive for both anxiety and depressive disorders (Supplementary Table 4; https://www.samedical.org/file/2244). Most of those women were aged 25 - 34 years (*n*=24; 60.0%), had been suffering from infertility for 1 - 5 years (*n*=26; 65.0%), were married (*n*=20; 50.0%), of whom 18 (90.0%) were in a monogamous marriage, had achieved Grade 8 - 12 level of education(*n*=28; 70.0%) or tertiary education (*n*=7; 17.5%) and were suffering from secondary infertility (*n*=23; 57.5%). The level of education was not significantly associated with a combination of depression and anxiety disorder.

Discussion

To the authors' knowledge, this is the first study conducted in SA that succeeded in identifying the presence of mental disorders in infertile women attending the Infertility Clinic at Universitas Academic Hospital. The study included mostly women at their reproductive peak,

Table 3. Patient Health Questionnaire (PHQ-9) scores by socio-demographic characteristics

	PHQ-9 score		
Variable	**Yes ≥10 (*n*=53) *n* (%)**	**No <10 (*n*=47) *n* (%)**	***p*-value***
Age (years)			0.062
18 - 24	2 (3.8)	3 (6.4)	
25 - 34	34 (64.2)	19 (40.4)	
>35	17 (32.1)	25 (53.2)	
Duration of infertility (years)			0.30
1 - 5	33 (62.3)	28 (59.6)	
6 - 10	14 (26.4)	9 (19.1)	
>10	6 (11.3)	10 (21.3)	
Marital status			0.60
Single	11 (20.8)	8 (17.0)	
Married	28 (52.8)	30 (63.8)	
Widowed	1 (1.9)	1 (2.1)	
Divorced	0 (0)	1 (2.1)	
Engaged	13 (24.5)	7 (14.9)	
Type of marriage (*n*=58)			0.70
Monogamous	25 (89.3)	28 (93.3)	
Polygamous	3 (10.7)	2 (6.7)	
Level of education			0.025
None	2 (3.8)	0 (0)	
Grades 1 - 7	6 (11.3)	0 (0)	
Grades 8 - 12	33 (62.3)	30 (63.8)	
Tertiary level	12 (22.6)	17 (36.2)	
Employment			0.80
Unemployed	29 (54.7)	22 (46.8)	
Self-employed	4 (7.5)	4 (8.5)	
Employed	20 (37.7)	21 (44.7)	
Type of infertility‡			0.10
Primary	24 (45.3)	29 (61.7)	
Secondary	29 (54.7)	18 (38.3)	

*Fisher's exact test was used to analyse the data.
‡Primary – had never been pregnant; secondary – had been pregnant before.

aged 25 - 34 years. The findings revealed a 53.0% depression prevalence rate and an anxiety prevalence of 50.0%, which were comparable with studies conducted in other developing countries. A depression prevalence of 52.7% was found in Nigeria,[5] while in a systemic review and meta-analysis by Kiani *et al*.,[12] the prevalence of anxiety symptoms in infertile women was 54% in low- and middle-income countries. In another Nigerian study,[13] an association between depression and primary infertility was reported. In Iran, Maroufizadeg *et al*.[8] found a depression prevalence of 33.0% and an anxiety prevalence of 49.6%, both lower than in our study. However, they used the Hospital Anxiety and Depression Scale (HADS) rather than the Generalized Anxiety Disorder (GAD) used in the current study.

In our study, 29 (64.4%) of 45 women who had been suffering from infertility for a duration of 1 - 5 years presented with moderate to moderately severe depression symptoms. These women might have been new to the infertility treatment programmes and were likely concerned about whether the therapy would have a positive outcome.

A significant association was found between the level of education of at least Grade 8 and the presence of depression. It might be questioned whether this association could be related to the stress caused by knowing the long and uncertain outcome of infertility treatment. In the authors' opinion, it is possible that educated patients have more knowledge of the high cost of infertility treatment, the risks or complications associated with infertility treatment and the possibility of failing to achieve a successful pregnancy despite the treatment. However, contrary to our findings, several studies reported an inverted association between infertility-related mental health and level of education.[14-16]

Approximately a quarter (24.0%) of the participants had moderate to severe levels of anxiety. It could be argued that these women were likely recently married and had just started their own families or had recurrent miscarriages or poor previous obstetric outcomes. Furthermore, many of them were educated and at the start of their careers, while they were failing to achieve the crucial societal role of reproduction, which could have resulted in anxiety about the future. However, this argument might be speculative, as there was no statistically significant association between anxiety and any of the sociodemographic elements examined in this study.

The fact that 40.0% of the study participants screened positive for both anxiety and depression could indicate the possibility of concomitant mental disorders in women attending the Infertility Clinic. Receiving a diagnosis of infertility is an emotional experience and may have several psychological consequences.[17] The actual occurrence of psychiatric conditions among women struggling with infertility is undeniably underestimated.[18] Furthermore, psychiatric disorders are often unnoticed or misdiagnosed in many infertile patients.[19,20] Addressing these shortcomings could contribute to achieving a better treatment outcome for patients. We did not find any association between those participants who screened positive for both depression and anxiety and any of the sociodemographic factors examined in the study.

Study limitations

Some limitations of the study should be considered. First, this was a cross-sectional study, which does not allow us to establish causal inferences between the study variables. Second, a larger sample size could be beneficial and might have been more representative. Third, we did not ascertain whether patients had experienced previous treatment failures, and how long they had suspected that they might have infertility problems before seeking medical attention, which might have assisted in explaining some of the findings. Lastly, the presence of these psychological disorders could also have been investigated in the participants' male partners. Generally, infertility causes and treatment options involve both partners, hence the partners would not be expected to be exempt from suffering from the same psychological morbidities found in our study participants.

Conclusion

The findings of this study exposed the relatively high prevalence of depression and anxiety among infertile women attending the Infertility Clinic at Universitas Academic Hospital. These are psychological morbidities that are often not screened for, despite being known to be associated with infertility in both women and men undergoing infertility treatment. We strongly recommend a shift in how female patients are treated at infertility clinics, that screening for these mental disorders is performed from the initial patient assessment and that patients are referred to mental health practitioners who can provide ongoing support from the start of infertility treatment. Referring patients to mental health practitioners will result in a more holistic patient care approach and possibly better infertility treatment outcomes.

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Data availability statement. Data are available from the corresponding author upon reasonable request.

Conflicts of interest. None.

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