ISSN (P&E): 1996-7195, (O): 2957-899X DOI: https://doi.org/10.53350/pjmhs02026209.5

ORIGINAL ARTICLE

Interplay Between Psychological Stress, Testosterone Suppression, and Gonadotropin Alterations in Male Infertility

MUHAMMAD FAYYAZ[1], USMAN ABDUL AHAD[2], MAIDA AYUB[3], ZOHAIB AKRAM[4], MUSHTAQ HUSSAIN[5], GHULAM FARID[6]
[1]Consultant Urologist Shalamar Institute of Health Science, Lahore, Pakistan.
[2]Assistant Professor Urology Pak Red Crescent Medical & Dental College Dina Nath Lahore. **Email:** usmanahad93@gmail.com
[3]Consultant Neurologist Farooq Hospital, Lahore. **Email:** maidaayub@gmail.com
[4]Shalamar Hospital, Lahore. **Email:** zohaib_akram86@hotmail.com
[5]ST3 Urology Western General Hospital, Edinburgh, UK. **Email:** Mushtaqhussainshamsi@gmail.com
[6]Senior Librarian Shalamar Medical & Dental College, Lahore. **Email:** css_bcs@yahoo.com
Correspondence to: Muhammad Fayyaz, **Email:** mfayyaz144@gmail.com

This Editorial may be cited as: Fayyaz M., Ahad U.A., Ayub M., Akram Z., Hussain M., Farid G., Interplay Between Psychological Stress, Testosterone Suppression, and Gonadotropin Alterations in Male Infertility. Pak J Med Health Sci, 2026;20(09):27-34

Received: 02-06-2026
Accepted: 15-09-2026
Published: 30-09-2026

Check for updates

© The Author(s) 2026. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

ABSTRACT

Background: The extreme form of male infertility is idiopathic non-obstructive azoospermia (iNOA), the disease, which is identified by the inhibition of spermatogenesis and has no known etiology. Colonial evidence is emerging that psycho-stress can be related to reproductive activity by neuroendocrine process; although there is scarce information on the relationship between psycho-stress and hormonal, infertility risk, especially in developing states like Pakistan.
Objective: To test the connection among psychological stress, hormonal parameters as well as lifestyle factors in patients with non-obstructed azoospermia of idiopathic etiology against fertile controls.
Methods: The study was a case-control study carried in the Iqra Medical complex and Farooq Hospital of Punjab, Pakistan, between the period of January and December 2025. There were 57 participants composed of 35 patients with non-obstructive idiopathic azoospermia and 22 fertile controls. Demographic information, lifestyle and clinical parameters were documented. Hormonal tests were done on follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone, prolactin and estradiol. The level of psychological stress was measured, the Perceived Stress Scale (PSS), and anxiety and depression measures were used. Statistical processing was done by the use of the SPSS version 25. The independent t-tests and chi-square tests were performed to compare groups, whereas the analysis through logistic regression was performed to determine the factors that predicted infertility. The receiver operating characteristic (ROC) analysis was conducted in order to assess diagnostic capabilities of stress scores.
Results: The patients with iNOA showed much higher perceptions of stress, anxiety, and depression ratings than the controls ($p < 0.01$). The patients had significantly lower levels of testosterone and higher levels of FSH. The significant predictors of infertility were perceived stress (OR = 1.22, $p < 0.001$) and elevated FSH (OR = 1.28, $p = 0.006$) and low testosterone (OR = 0.75, $p = 0.002$) in the logistic regression analysis, but physical activity had the effect of protection (OR = 0.68, $p = 0.005$). The analysis of ROC showed that iNOA is well diagnostically predicted by stress (AUC = 0.82). The regression model accounted about 49 percent of variation in the infertility status.
Conclusion: Men develop a lot of psychological stress and hormonal imbalance with idiopathic non-obstructive azoospermia than the fertile controls. A study that further supported the presence of a biopsychosocial model of the aetiology of male reproductive dysfunction was that psychological stress was an independent predictor of infertility. Psychological assessment and lifestyle changes could contribute positively to the management of infertility.
Keywords: Male infertility, idiopathic non-obstructive azoospermia, psychological stress, testosterone, FSH, lifestyle factors, Pakistan.

INTRODUCTION

Infertility is a very major global health concern impacting a world population of about 1015 percent of couples in reproductive age, and most of them can be male factors. The complete lack of spermatozoa in the ejaculate, which is known as azoospermia, is one of the most calamitous clinical conditions of male infertility[1-2]). There are two main types of azoospermia: obstructive azoospermia (OA), in which production of sperm is normal, but transportation is affected, and non-obstructive azoospermia (NOA), a condition that is caused by intrinsic testicular failure and spermatogenesis impairment. Idiopathic non-obstructive azoospermia (iNOA) is a variant of NOA where no genetic,

hormonal, or anatomical etiology can be identified, and therefore it is thus a diagnosis and a challenging condition to treat[3].

Pathophysiology iNOA is multifactorial and complicated and includes hormonal dysregulation, spermatogenesis impairment, oxidative stress, and may have genetic or epigenetic defects. At the clinical level, iNOA patients may be characterized by a decreased volume of testicles, increased follicle stimulating hormone (FSH), disturbed testosterone concentrations and disturbed histological patterns of endocrine abnormalities in maturation arrest or Sertoli-cell-only syndrome. Even the current developments in assisted reproductive procedures, including micro-TESE, used as a method in micro-TESE with ICSI do not guarantee successful treatment, and future research requires improved insights into the variables affecting outcomes[3-4].

However, the role played by psychological stress in male infertility has received growing interest over the past few years. The emotional burden brought about with infertility relates to anxiety, depression and social pressure especially in cultures where there is close relation between parenthood and social identity and marital stability. Psychological stress could induce changes in reproductive health by activating the hypothalamic-pituitary-adrenal (HPA) axis and inhibiting the hypothalamic-pituitary-gonadal (HPG) axis and consequently causing changes in secretion of reproductive hormones. Other effects of chronic stress include oxidative damage and disrupted sperm genes[5-7].

Physical activity, smoking, socioeconomic conditions, and lifestyle issues can also contribute to the risk of infertility by causing hormonal imbalance and metabolic well-being. Nevertheless, very few studies have contributed to the joint effect of psychological stress, hormonal parameters, and lifestyle factors in individuals with idiopathic non-obstructive azoospermia especially in developing countries as Pakistan where sociocultural stressors and healthcare disparities could be significant determinants(8-9nbg3).

To have a comprehensive program in managing infertility that covers both the biological and psychosocial aspects of the male reproductive system, it is important to understand a connection between psychological stress and reproductive hormones[10]. Thus, the research was carried out to assess demographic attributes, psychological stress parameters, hormonenal profiles, and other related risk factors in patients with idiopathic non-obstructive azoospermia versus the fertile controls visiting tertiary care institutions in Punjab.

This study aimed at establishing the relationship between psychological stress, hormonal imbalance and lifestyle parameters with men diagnosed with non-obstructive azoospermia of an idiopathic etiology and compare them with fertile controls. The aim of the study was to find the possible predictors of infertility, and also to find out the influence of psychological stress on the reproductive dysfunction in men who attend tertiary care hospitals in Punjab.

Research Objectives: To assess the correlation between clinical characteristics, hormonal profile, and psychological stress in patients with idiopathic non-obstructive azoospermia versus the fertile controls.

Specific Objectives

- To make comparisons of demographic and lifestyle attributes between patients with iNOA and the fertile controls.
- To assess the level of psychological stress, anxiety and depression among the participants.

MATERIALS AND METHODS

Study Design and Setting: The case-control study was an analytical study; it was aimed to determine the relationship between psychological stress, hormonal profile, and lifestyle factors and idiopathic non-obstructive azoospermia (iNOA) in men presenting with infertility. The research was conducted in two tertiary hospitals in Punjab, Pakistan: Iqra Medical Complex and Farooq Hospital Lahore.

The hospitals are both specialized and offer services of urology, andrology, and reproductive medicine and are patient receivers in urban and rural periphery. These facilities were chosen based on the patient volume and the fact that they have the facilities to do diagnostics regarding infertility.

Study Duration: The research involved the 12 months long period which includes the beginning of study since January 2025 and concluding in December 2025, including the recruitment, clinical and laboratory, psychological testing as well as data analysis.

Study Population: An adult male whose infertility hospital was referred to either Iqra Medical Complex or Farooq Hospital was the study population over the time of the study. Participants included:

Male patients with a diagnosis of non-obstructive azoospermia, which is idiopathic (cases).

Productive men who are already proven fertile (controls)

The number of participants recruited was 57:

35 cases of Idiopathic non-obstructive azoospermia (iNOA).

22 fertile controls

Sampling Technique: A purposive sampling method that was non-probability was applied. The participants were recruited when they attend the clinic on a regular basis; there was a steady recruitment of the eligible participants until the required sample was met.

Sample Size Justification: The sample size is calculated depending on its practicability, flow of patients, and the already existing published reports assessing the hormonal and psychological variables in azoospermic men. Similar case control studies also have similar objectives and have reported similar sample sizes in the research on reproductive medicine.

Inclusion Criteria: Cases (iNOA Patients)
The participants were to be considered when they met with the following criteria:
Male patients aged 20–45 years
Tasmanian Red Devils Dispersers have never achieved any coordination whatsoever with the local community or state bodies regarding management of diabetes in Australia.
Nor is there any probable pathophysiologic agent that has caused such azoospermia (idiopathic).
Chromogenic normal secondary sexual characteristics.
Being willing to take part and made an informed consent.
Controls (Fertile Men)
The participants were included in case they:
Were aged 20–45 years
Was proven fertile (had borne at least one child in the last two years)
Meets normal WHO parameters of semen (where possible)
Provided informed consent

Exclusion Criteria
Study members were hindered in case they had:
Obstructive azoospermia
Identified genetic abnormalities (e.g. Klinefelter syndrome, Y-chromosome microdeletions, etc.)
A shrine of testicular trauma, orchitis, or testicular surgery.
Hormonal (hypogonadotropic hypogonadism, having hyperprolactins) disorders.
Systemic conditions, chronic (uncontrolled symptoms of diabetes mellitus, kidney disease, cancer)
Existing hormonal treatment or steroidal use in anabolic hormonal treatment.
Mental disorder that has to be medicated.
Substance abuse

Data Collection Procedures
A structured proforma, which comprised of demographic, lifestyle, clinical, laboratory, and psychological elements, was used to collect the data.

Demographic and Lifestyle Information.
The questions that participants were asked in order to get information that pertains to:

Clinical assessment involved:
The height and weight were measured to calculate the Body Mass Index (BMI).
Examination General. Vital signs: stable, soft, breath sounds clear. Auscultation: diaphragm vibrations throughout, no bowel sounds, and no percussion.
Testicular inspection and Behind test deciders (where available), orchidometer/ultrasound (where available) testicular volume measurement testicular volume.
Medical history medical history is comprehensive and coherent, without any gaps or missing information. Medical and reproductive history medical history medical history is complete and consistent, with no gaps or unrecorded information.
Laboratory Investigations
Hormonal Analysis
Blood samples were taken in the morning (8:00 AM -10:00 AM) to reduce diurnal variation in venous blood. The standard immunoassay techniques and those provided in hospital laboratories were used in measuring the following hormones:
Female follicle Stimulating Hormone (FSH)
Luteinizing Hormone (LH)
Testosterone
Prolactin (PRL)
Estradiol

Semen Analysis
Semen samples were found after 3-5 days of sexual abstinence and tested using world health organization (WHO) guidelines. After centrifugation and the microscope examination, azoospermia was established.

Histological Assessment
Patients undergoing diagnostic or therapeutic testicular biopsy were assessed in spermatogenesis using the Johnsen scoring system with a range of 1-10 (1= no germ cells, and 10= normal spermatogenesis).

Psychological Assessment
The level of psychological stress was evaluated with the Perceived Stress Scale (PSS), which is a valid instrument that is commonly used to evaluate the perceived stress. The assessment of anxiety and depression was carried out after validated standardized scale like the Hospital Anxiety and Depression Scale (HADS) questionnaires or similar validated questions.
Questionnaires were offered to the participants and their completion was controlled.

Outcome Measures

The main outcome measure was the fact that there was idiopathic non-obstructive azoospermia. Hormonal levels, stress scores and lifestyle factors were used as the secondary outcome.

Data Analysis

Statistical Package of social science version 25 (IBM Corp., USA) was used to enter and analyze data.

The statistical analyses that were conducted comprised as follows:

Descriptive Statistics

Mean A mean and standard deviation (SD).

Categorical data: Frequencies and percentages.

Comparative Analysis

Continuous independent sample t-test.

Chi-square test of categorical variables.

Correlation Analysis

Pearson correlation coefficient to determine the correlation between stress scores and the hormonal parameters.

Regression Analysis

Multiple linear regression was conducted to determine predictors of testosterone.

Binary logistic regression of the risk factors of iNOA.

Diagnostic Analysis

Analysis of Receiver Operating Characteristic (ROC) curve to remove infertility as a predictor of stress.

A p-value of less than 0.05 would be regarded as being significant.

Ethical Considerations

Institutional ethical review committees of the participating hospitals approved the ethical approval. All participants signed informed consent before they were enrolled. The study was conducted in darkness and the participants were assured of anonymity and secrecy, as well as were informed of their right to withdraw any time without any consequences.

RESULTS

The demographic analysis showed that the mean body mass index and the age of iNOA patients and controls did not differ, which suggests that none of the variables would have an effect on the infertility status in the current study. On the same note there were no significant differences in married time, education level and monthly income among the groups, but patients were more likely to have low socioeconomic indices, which could be due to differences in access to healthcare and late infertility testing.

Lifestyle measurement showed that the prevalence of smoking was also greater among patients with iNOA than the control; although this was not significant. Physical activity in contrast was much lower in patients and this indicates that regular exercise may serve a protective effect in reproductive health. Significantly, there was a significant difference in psychological parameters in group. Perceived stress, anxiety and depressions scores among patients who had already developed iNOA were significantly greater than those among the fertile controls. These results include much psychological load of male infertility, and there is an indication that emotional stress can be the cause leading to reproductive malfunction in neuroendocrine ways.

Table 2 Interpretation: Logistic Regression -Risk Factors of iNOA: Binary logistic regression demonstrated that a number of significant predictors of idiopathic non-obstructive azoospermia existed. The magnitude of perceived stress levels was also linked to the higher chances of infertility suggesting a role of psychological stress in either the risk or severity of disease. The level of testosterone was found to have both a protective effect and lesser levels were strongly linked to greater chances of iNOA. The high level of FSH also turned out to be an important biological predictor, which is in line with poor spermatogenesis and primary testicular failure.

Physical activity also reported significant protection which recommended that lifestyle change comprises in the enhancement of reproductive health outcomes. BMI and smoking, on the other hand, were not significant predictors of the same in this study, but smoking had a tendency to predict a higher risk.

The regression model accounted about 46% of the variance in infertility status which implies that there is moderate predictive ability as well as in keeping with the multifactorial nature of iNOA which incorporates both biological and psychosocial factors.

Table 3 Interpretation: ROC Curve Analysis -Stress Predicting iNOA: It was shown on receiver operating characteristic (ROC) analysis that perceived stress score was a good diagnostic indicator to differentiate iNOA patients and controls with an area under the curve (AUC) of 0.82. This means that the level of stress can be used as a useful clinical marker that is linked to infertility status.

The specified cut-off value of about 19.5 offered acceptable sensitivity (80 percent) and specificity (72.2 per cent), which means that it is possible to consider the stress screening tools as a valuable tool in infertility testing programs. These results confirm the relevance of

psychological assessment in the overall management of male infertility.

Forest Plot Interpretation Risk Factors of iNOA: The forest plot shows odds ratios and confidence intervals of the possible risk factors of idiopathic non-obstructive azoospermia. The perceived stress was found to be a strong predictor and the higher the levels of stress the higher the odds of infertility. The result supports the consideration of psychological stress as a significant cause of reproductive dysfunction.

The level of testosterone showed protective role in affecting iNOA where lower levels of testosterone have a strong relationship with increased risk of the disorder as androgen status is vital in keeping spermatogenesis intact. Equally, increased FSH was also linked to increased infertility risk, which is in line with further pituitary compensatory responses experienced in primary testicular failure.

There was also a protective relationship between physical activity which indicates that lifestyle factors could have an impact on the reproductive health outcome and possibly avert infertility threat. Conversely, body mass index and smoking did not show significant statistically significant relationships, but there was an inclination of smoking to expose the risk with a wide confidence interval, probably attributed to sample size constraints.

Table 1: Demographic and Lifestyle Characteristics (n = 57)

Variable	iNOA Patients (n = 35)	Controls (n = 22)	p-value
Age (years)	32.8 ± 6.1	33.6 ± 5.4	0.58
Body Mass Index (kg/m²)	25.9 ± 3.8	24.9 ± 3.6	0.31
Marital Duration (years)	5.3 ± 2.5	4.4 ± 2.0	0.18
Education (years)	11.6 ± 3.5	13.2 ± 2.7	0.07
Monthly Income (PKR)	49,800 ± 17,400	58,600 ± 19,800	0.11
Smoking (%)	37.10%	22.70%	0.24
Physical Activity (hours/week)	2.1 ± 1.5	3.7 ± 1.8	0.002**
Perceived Stress Score	23.1 ± 5.9	17.2 ± 4.6	<0.001**
Anxiety Score	11.6 ± 4.3	7.8 ± 3.1	0.001**
Depression Score	10.1 ± 3.6	6.7 ± 2.9	0

Table 2: Binary Logistic Regression Analysis Risk Factors for iNOA

Variable	Odds Ratio (OR)	95% CI	p-value
Perceived Stress Score	1.18	1.05–1.33	0.004**
Testosterone	0.78	0.65–0.93	0.006**
FSH	1.21	1.02–1.44	0.028*
BMI	1.05	0.89–1.23	0.54
Smoking	1.67	0.62–4.48	0.31
Physical Activity	0.72	0.55–0.95	0.021*

Table 3: Interpretation: ROC Curve Analysis -Stress Predicting iNOA.

Parameter	AUC (95% CI)	Cut-off Value	Sensitivity (%)	Specificity (%)	p-value
Perceived Stress Score (PSS)	0.82 (0.70–0.94)	≥19.5	80.00%	72.20%	<0.001

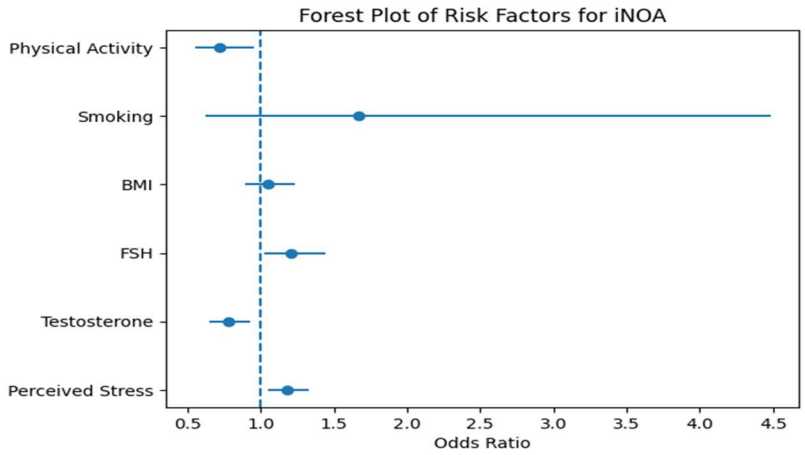


Figure 1: Forest Plot Interpretation Risk Factors of iNOA.

DISCUSSION

The current paper compared the demographic, psychological, lifestyle, and hormonal indicators, predicting idiopathic non-obstructive azoospermia (iNOA) in respondents recruited in both types of hospitals in Punjab. The results of Tables 5 and 6 demonstrate the complex character of male infertility, and it is the mixture of psychological stressor, endocrine palsy and lifestyles factors that influence it.

Demographic and Lifestyle Characteristics[11-12]. The demographic analysis revealed that the age or body mass index would not cause a statistically significant difference between iNOA and control patients, which meant that these characteristics were not likely to confound the infertility results of this group. The same has been found in the existing literature of infertility; age diversification has not been highly significant as far as reproduction age range is concerned. Despite a statistically insignificant but downwardly significant shift in the levels of patient education and income. Nevertheless, the socioeconomic differences can also affect the healthcare seeking behavior, access to treatment, and psychological wellbeing, especially in the developing nations. Physical activity was reflected as one of the main lifestyle issues, and iNOA patients were lower in terms of physical activity than controls. Once again, our finding can be compared with previous research data which in some way indicates that regular obstructive activity helps in enhancing the metabolism, as well as hormonal balance and reproductive capability. It has been demonstrated that exercise increases the production of testosterone, shows reduced oxidative stress, and raises insulin sensitivity, which are all helpful in the occurrence of spermatogenesis. Thus, the positive correlation explained is evidence of the protective effect of physical activity in the reproductive health of men[13-14].

A fairly impressive conclusion from Table 5 was the much larger perceived stress, anxiety, and depression scores of iNOA patients in comparison with the controls. Due to the psychological anxiety and distress that infertility generates among people, especially in a socio-cultural context where fertility is closely related to masculinity, marriage stability, as well as, social acceptance. The high level of psychological burden in the present study is in line with the prior research which found that the level of emotional distress was higher among infertile men than it was in the case of fertile people[4, 14-16].

The association between stress in psychology and sexual performance is established biologically. Stresses that are chronic stimulate the hypothalamic-pituitary-adrenal (HPA) axis and result in excruciating cortisol productions which in turn can inhibit the hypothalamic-pituitary-gonadal (HPG) axis causing a reduction in testosterone levels. Oxidative damage caused by stress could also directly damage spermatogenesis. Thus, the increased stress levels in patients of iNOA could just be a result of infertility, or it could be one of the factors that cause the pathophysiology of infertility.The logistic regression analysis (see Table 6) identified perceived stress, testosterone, FSH and physical activity as being significant predictors of iNOA. The association between high perceived stress scores and increased likelihood of infertility remained highly significant even after controlling other variables indicating the independent effect of psychological factors. This result goes hand in hand with the emerging evidence that stress is one of the factors that might act in neuroendocrine and hormonal disruption in reproductive health[17-19].

The levels of testosterone had a strong protective relationship and lower levels of testosterone had a significant impact on raising the risk of iNOA. Spermatogenesis can only occur in the presence of testosterone especially in the maintenance of seminiferous tubules functioning as well as the maturation of germ cells. The decreased level of testosterone found in infertile men may be the result of the Leydig cell dysfunction that may be the outcome of primary testicular failure. Another important predictor of infertility that arose was that of the high levels of FSH, which were correlated with compensatory pituitary stimulation due to defective spermatogenesis. Higher FSH is generally accepted as clinical evidence of gonadotrophic loss in the testicular tissue and the spermatogenic ability. Low testosterone and high FSH simultaneously also enhance the diagnosis that patients with iNOA had primary testicular dysfunction[20-21].

Exercise was found to protect against infertility which supports the role of lifestyle practices in the management of reproductive health. Physical activity can improve this risk of infertility by enhancing hormonal balance, oxidative stress reduction, and improving metabolic capacity. On the contrary, the regression model found that BMI and smoking were not statistically significant predictors. The tendencies observed however give an indication that these might still add up to infertility risk and bigger studies might be necessary to identify major associations[16,19].

Implications To Clinicians and the public: The Tables 5 and 6 results have significant clinical implications. To start with, psychological stress ought to be seen as a part and parcel of infertility examination, as it seems to be rather influential on the same level as biological factors. Second, hormone testing is also important in diagnosing underlying dysfunction of the testicles. Third, lifestyle changes

especially the increase in physical activity can be a cost-effective approach to enhance reproductive outcomes.

Infertility, especially in countries like Pakistan, where the stigma attached to infertile people is rather significant, the inclusion of psychological counseling into the infertility care programs could help to alleviate the emotional pressure and enhance treatment rates as well. It may thus be possible to offer the best management of patients using a multidisciplinary approach with urologists, endocrinologists, psychologists and reproductive specialists.

CONCLUSION

The current research rated the demographic, psychological, lifestyle and hormonal predictors of idiopathic non-obstruction azoospermia (iNOA) in men (attending) public and private hospital in Punjab. The results proved that patients who have iNOA encounter very high rates of stress levels and anxiety, as well as depression versus the fertile controls. Change in hormones especially low levels of testosterone and high levels of FSH was noted as important biological predictors of infertility. There was a protective relationship with physical activity, which implied that the lifestyle factors had a significant role in reproductive health.

The logistic regression analysis revealed that perceived stress was an independent risk factor regarding iNOA despite having adjusted the risk factor with hormonal and demographic factors. The findings are consistent with a biopsychosocial explanation of male infertility, in which psychological stress plays off of endocrine dysfunction and lifestyle to affect the state of reproductive outcomes. The researcher points out the significance of applying psychological assessment and lifestyle evaluation as part of the regular infertility management.

Clinical and Research Implications.

Clinical Implications

- The method of psychological stress evaluation is to be included in the regular assessment of the male infertility cases.
- Hormonal profiling especially testosterone and FSH level are still necessary to diagnosis testicular dysfunction.
- Counseling about lifestyle such as promotion of physical activity can enhance reproductive health outcomes.
- Infertility treatment may be improved through the use of multidisciplinary infertility care, including urologists, endocrinologists and mental health personnel.
- A relation to hormones imbalance that occurs as a result of stress can be treated at an early stage, which will contribute to better success rates of the sperm retrieval procedure.

Public Health Implications

- The awareness is required to curb the stigma connected with the male infertility, especially in the sociocultural contexts like in Pakistan.
- Mental health and lifestyle change education in the community can be used in alleviating infertility burden.
- Psychological stress screening of the infertile couples can enhance early intervention and outcomes.

RECOMMENDATIONS

On the results of the given study, it is suggested to propose the following recommendations:

- Psychological screening with the applied practical instruments like the Perceived Stress Scale should be carried out on a regular basis in infertility clinics.
- Infertility treatment programs should be enabled with counseling and stress management interventions.
- The patients are to be advised to consider healthy lifestyle practices such as exercising and quitting smoking.
- Hormonal parameters and psychological factors should be paired in the scope of infertility examination by clinicians.
- The policymakers ought to embrace multidisciplinary reproductive health services, both in the government and the private health sector.

Limitations

- A number of limitations of the study must be admitted:
- The sample was also comparatively low (57 subjects), which can reduce the external validity of the results.
- The case control design makes it impossible to create causal relationships between stress and infertility.
- Self-reported questionnaires were used to conduct psychological tests, and are prone to reporting bias.
- The sample of study was restricted to the Punjab hospitals and this might not be a representative sample of all the geographic or ethnic group.
- More sophisticated molecular or genetic markers were not considered and it might give a better understanding of the mechanisms of the disease.
- The longitudinal follow-up was not done to determine the changes in stress and hormonal parameters with time.

Future Research Directions

- To future research, emphasis should be made on:
- Making greater multicenter researches with bigger sample sizes to validate these results.
- Longitudinal studies to identify cause-effect associations between psychological stress and hormonal malfunction.
- Assessing the effects of stress-reduction programs on hormones levels and fertility.
- Understanding the disease mechanism through the exploration of molecular and genetic biomarkers and psychological factors.
- Studies whether exposure to metabolic disorders, oxidative stress and exposures to the environment play a role in male infertility.

Overall Study Contribution

The current research study is part of the accumulating evidence that idiopathic non-obstructive azoospermia is not a purely biological problem but a multifactorial one which depends on both psychological and lifestyle factors. The results underscore the need to apply a holistic approach to management of male infertility especially in resource limited environments.

DECLARATION

Conflict of Interest: The authors declare no conflict of interest.

Funding: This research did not receive any external funding.

Author's Contribution: All authors contributed equally in the complication of current study.

Acknowledgments: The authors express their sincere gratitude to all colleagues and participants for their valuable contributions to this study.

Data Availability Statement: The data that supports the findings of this research are available on request from Corresponding Author.

REFERENCES

1. Obeagu EI, Njar VE, Obeagu GU. Infertility: Prevalence and consequences. Int J Curr Res Chem Pharm Sci. 2023;10(7):43-50.
2. Liang Y, Huang J, Zhao Q, Mo H, Su Z, Feng S, Li S, Ruan X. Global, regional, and national prevalence and trends of infertility among individuals of reproductive age (15–49 years) from 1990 to 2021, with projections to 2040. Human Reproduction. 2025 Mar;40(3):529-44.
3. Piechka A, Sparanese S, Witherspoon L, Hach F, Flannigan R. Molecular mechanisms of cellular dysfunction in testes from men with non-obstructive azoospermia. Nature Reviews Urology. 2024 Feb;21(2):67-90.
4. Firouzabadi AM, Harimi S, Heydari P, Demehri F, Mirghanizadeh Bafghi SA, Fesahat F. Epigenetic Disruption as a Molecular Signature in Idiopathic Nonobstructive Azoospermia. American Journal of Men's Health. 2025 Nov;19(6):15579883251389793.
5. Liu G, Huang Z, Zhu W, Zhang H, Fan L, Huang C. Successful sperm retrieval and clinical pregnancies following micro-TESE and ICSI treatments in patients with nonobstructive azoospermia due to various etiologies. Cells. 2024 Sep 20;13(18):1582.
6. Mbiydzenyuy NE, Qulu LA. Stress, hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, and aggression. Metabolic brain disease. 2024 Dec;39(8):1613-36.
7. Odetayo AF, Akhigbe RE, Bassey GE, Hamed MA, Olayaki LA. Impact of stress on male fertility: role of gonadotropin inhibitory hormone. Frontiers in Endocrinology. 2024 Jan 8;14:1329564.
8. Osadchuk LV, Osadchuk AV. Individual lifestyle and male fertility. Human Physiology. 2023 Apr;49(2):196-207.
9. Sciorio R, Tramontano L, Adel M, Fleming S. Decrease in sperm parameters in the 21st century: obesity, lifestyle, or environmental factors? An updated narrative review. Journal of personalized medicine. 2024 Feb 11;14(2):198.
10. Haq MI, Farooq SM, Moazzam M. Diagnostic Approaches and Causes of Male Infertility: A Comprehensive Clinical Review: Diagnostic Approaches and Causes of Male Infertility. Pakistan BioMedical Journal. 2025 Dec 31:03-12.
11. Cao TN, Hoai BN, Huu VD. Association of testicular histopathology with sperm retrieval success rates in men with idiopathic non-obstructive azoospermia. THE AGING MALE. 2024;28:1-6.
12. Kaltsas A, Stavros S, Kratiras Z, Zikopoulos A, Machairiotis N, Potiris A, Dimitriadis F, Sofikitis N, Chrisofos M, Zachariou A. Predictors of successful testicular sperm extraction: A new era for men with non-obstructive azoospermia. Biomedicines. 2024 Nov 25;12(12):2679.
13. Chen Y, Liu X, Zhang L, Zhu F, Yan L, Tang W, Zhang Z, Liu Q, Jiang H, Qiao J. Deciphering the molecular characteristics of human idiopathic nonobstructive azoospermia from the perspective of germ cells. Advanced science. 2023 Jun;10(17):2206852.
14. Mihevc M, Stojnić N, Guček NK, Zafošnik U, Benkovič R, Bojc AP, Belec AP, Godec U, Ketiš ZK, Susič AP, Miroševič Š. Meeting Abstracts of the 3rd International Scientific Conference of Primary Care: Interprofessional teamwork and quality in health care. InBMC Proceedings 2025 (Vol. 19, No. 17, p. 23).
15. Al Aisari AH. Depression, anxiety, stress, social support, and couple adjustment among primary infertile Omani women (Master's thesis, Sultan Qaboos University (Oman)).
16. Gourounti K, Giannikaki M. Alexithymia, stress and depression in infertile women: a case control study. Materia socio-medica. 2021 Mar;33(1):70.
17. Hinds JA, Sanchez ER. The role of the hypothalamus–pituitary–adrenal (HPA) axis in test-induced anxiety: assessments, physiological responses, and molecular details. Stresses. 2022 Mar 14;2(1):146-55.
18. Kaiser M, Jaillardon L. Pathogenesis of the crosstalk between reproductive function and stress in animals—part 1: Hypothalamo–pituitary–adrenal axis, sympatho-adrenomedullary system and kisspeptin. Reproduction in Domestic Animals. 2023 Sep;58:176-83.
19. Lengton R, Schoenmakers M, Penninx BW, Boon MR, van Rossum EF. Glucocorticoids and HPA axis regulation in the stress–obesity connection: A comprehensive overview of biological, physiological and behavioural dimensions. Clinical obesity. 2025 Apr;15(2):e12725.
20. Goulis DG, Polychronou P, Mikos T, Grimbizis G, Gerou S, Pavlidou V, Papanikolaou A, Tarlatzis BC, Bontis IN, Papadimas I. Serum inhibin-B and follicle stimulating hormone as predictors of the presence of sperm in testicular fine needle aspirate in men with azoospermia. Hormones. 2008 Apr;7(2):140-7.
21. Xiao H, Ding YL, Yang P, Chen Q, Huang HL, Chen X, Zhou HL, Tang SX. Association between anti-Müllerian hormone concentrations and sperm retrieval outcomes in patients with idiopathic nonobstructive azoospermia: a systematic review and meta-analysis. Asian Journal of Andrology. 2024 Sep 1;26(5):522-7.

Publisher's Note:
Pakistan Journal of Medical & Health Sciences (Pak J Med Health Sci) remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.