

Investigation of the relationship between sexual and mental health indices in women with diabetes and its association with biochemical features using machine learning

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Abstract

Diabetes mellitus is often accompanied by psychological distress and sexual dysfunction, yet the complex relationships between these outcomes and biochemical characteristics in women remain insufficiently understood. This cross-sectional study, using a data-mining approach, examined the associations between sexual and mental health indices and metabolic and biochemical markers in 124 reproductive-aged women with type 2 diabetes. Sexual function was assessed using the Female Sexual Function Index (FSFI), psychological status was evaluated with the Depression, Anxiety, and Stress Scale-21 (DASS-21), and biochemical measures included fasting blood glucose, glycated hemoglobin (HbA1c), two-hour postprandial glucose (2HPP), and lipid profile components. The findings showed that most participants had impaired sexual function, particularly in the domains of desire, arousal, lubrication, and pain, while considerable levels of depression, anxiety, and stress were also observed. Data-mining analyses and machine learning models identified 2HPP as the most important glycemic predictor of overall sexual function and several FSFI domains, whereas HbA1c showed the strongest associations with sexual desire and pain. Triglycerides emerged as the most important lipid predictor of both sexual and psychological health indices, while HDL demonstrated relatively protective associations. Mutual information analysis further revealed the greatest degree of shared information between triglycerides, VLDL, and the domains of sexual pain, stress, and depression. These findings underscore the central role of postprandial glucose dysregulation and dyslipidemia in the co-occurrence of sexual dysfunction and psychological distress in women with diabetes and suggest that data mining and machine learning may provide clinically meaningful insights into the complex metabolic, psychological, and sexual interactions underlying diabetes-related health outcomes.

Introduction

One of the most common chronic metabolic diseases in the world, diabetes mellitus (DM) has become a significant public health concern due to its steadily increasing prevalence. Over 400 million people worldwide are estimated to have diabetes, and this figure is expected to rise significantly over the next several decades (1). The multifaceted effects of diabetes from a physical, psychological, and social standpoint are made even more complicated by the fact that women, especially those of reproductive age, make up a sizable portion of the affected population (2).

The less evident aspects of diabetes, such as mental health and sexual function, have long been on the periphery of clinical and research attention, despite the fact that its metabolic effects and vascular complications are well known (3). Disorders of desire, arousal, lubrication, orgasm, sexual satisfaction, and pain are all included in the multifaceted concept of female sexual dysfunction (FSD). According to epidemiological data, the prevalence of FSD in women with type 2 diabetes is between 60 and 70 percent, which is much higher than in the general population (4, 5).

Sexual disorders in women with diabetes have been linked to a number of mechanisms, including systemic inflammation, endothelial dysfunction, decreased pelvic blood flow, peripheral neuropathy,

hormonal changes, and chronic hyperglycemia (6). These conditions are linked to poorer treatment compliance, a lower quality of life, and worsened diabetes clinical outcomes in addition to lowering the quality of marriages and sexual satisfaction (7).

Diabetes has a substantial impact on women's mental health in addition to sexual disorders. Numerous studies and meta-analyses have demonstrated that people with diabetes are almost twice as likely to experience depression as people without the disease, and that stress and anxiety are also more common in this group (8). Psychological disorders in diabetic patients are thought to be significantly predicted by factors like poor glycemic control, elevated body mass index (BMI), insulin resistance, longer disease duration, and the presence of chronic complications (9, 10). In this context, the Depression, Anxiety, and Stress Scale (DASS-21) has been extensively utilized as a valid, dependable, and frequently used tool for evaluating psychological status in clinical populations, including patients with diabetes (11).

Even though there is mounting evidence that sexual and psychological disorders are highly prevalent in women with diabetes, a large percentage of previous research has looked at these two areas independently. Additionally, there is still a dearth of research assessing psychological and sexual health in conjunction with metabolic and biochemical markers (12). The relationship between diabetes, mental health, and sexual function can be explained by biochemical markers like HbA1c, lipid profile, insulin resistance, and inflammatory markers, but there is still a research gap in this area (13, 14). However, the majority of earlier research has used traditional statistical methods, which are not very good at spotting intricate patterns, nonlinear relationships, and multivariate interactions. Data mining and machine learning techniques have become effective tools for deciphering complex clinical data in recent years, allowing for the identification of hidden patterns and more precise health outcome prediction (15). However, there hasn't been enough focus on using these methods to examine biochemical traits, psychological health, and sexual health in women with diabetes at the same time.

Therefore, using the Female Sexual Function Index (FSFI) and the DASS-21 scale, the current study was designed with the goal of thoroughly examining sexual and psychological health in women with Diabetes Mellitus and using data mining algorithms to analyze their association with biochemical and metabolic indicators. Obesity, insulin resistance, and poor metabolic control are thought to be linked to more serious sexual and psychological health issues. Determining these trends can help develop multifaceted, individualized intervention strategies for the treatment of diabetic women.

Methodology

In order to investigate the relationship between sexual and psychological health indicators and biochemical characteristics in women with diabetes during the reproductive period, a cross-sectional analytical study was carried out using a data mining approach. The Tarbiat Modares University Ethics Committee in Tehran, Iran, approved the research protocol. All participants were fully informed about the

goals and methods of the study prior to data collection, and written informed consent was acquired. Only the research team had access to the data, and each participant's information was kept private.

To investigate the relationship between sexual and psychological health indicators and biochemical characteristics in women with diabetes during the reproductive period, a cross-sectional analytical study was conducted using a data mining approach.

The research protocol was reviewed and approved by the Ethics Committee of Tarbiat Modares University, Tehran, Iran (ID IR.MODARES.REC.1403.016). All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee, the relevant national regulations, and the Declaration of Helsinki. All participants were fully informed about the objectives and procedures of the study prior to data collection, and written informed consent was obtained from all participants. Participation was voluntary, and participants had the right to withdraw at any time without any consequences. All data were anonymized prior to analysis. Only the research team had access to the dataset, and participants' confidentiality and privacy were strictly maintained throughout the study.

Study Population Recruitment:

This cross-sectional study was carried out at the Yazd Diabetes Specialized and Subspecialized Center between August 2024 and January 2025. Married women between the ages of 18 and 54 who had been diagnosed with type 2 diabetes for at least a year and whose diagnosis was verified using the American Diabetes Association's (ADA) criteria made up the study population (16). Diagnostic criteria included fulfillment of any one of the following:

1. Glycated hemoglobin (HbA1C) $\geq 6.5\%$
2. Fasting plasma glucose ≥ 126 mg/dL after a minimum of 8 hours of fasting
3. Two-hour plasma glucose ≥ 200 mg/dL following an oral glucose tolerance test with 75 g glucose load
4. Random plasma glucose ≥ 200 mg/dL in the presence of classic hyperglycemic symptoms

Inclusion and Exclusion Criteria:

Body mass index (BMI) between 18.5 and 30, non-insulin dependence, married status, confirmed diagnosis of type 2 diabetes based on ADA criteria (16), and willingness to fill out the sexual and psychological health questionnaires were among the inclusion criteria. Pregnancy or lactation, the use of drugs that impair sexual function (like phosphodiesterase inhibitors), the use of anxiety medications, and the occurrence of an acute stressful event within the previous year were all exclusion criteria.

Sexual and Psychological Function Assessment:

The Female Sexual Function Index (FSFI) questionnaire was used to evaluate the participants' sexual function. Designed to assess female sexual function over the previous four weeks, this standardized, validated, and popular tool has shown excellent validity and reliability in both domestic and international studies. Sexual desire (2 items), sexual arousal (4 items), vaginal lubrication (4 items), orgasm (3 items), sexual satisfaction (3 items), and pain during intercourse (3 items) are the six domains that make up the FSFI questionnaire's 19 items.

A five-point Likert scale is used to score each item; depending on the domain, the range for each item is either 0 to 5 or 1 to 5. The domain-specific coefficient is multiplied by the sum of the raw scores of the pertinent items to determine the domain scores. Sexual desire (0.6), arousal and vaginal lubrication (0.3), and orgasm, sexual satisfaction, and pain (0.4) are the domains' weighting coefficients.

As a result, each domain score falls between 0 and 6. The lowest and maximum scores for each domain are as follows: sexual desire is between 1 and 2, sexual satisfaction is between 0 and 6, and other domains are between 0 and 6. Higher scores indicate better sexual function. The total FSFI score, which ranges from 2 to 36, is calculated by adding the scores of all six domains.

On the overall FSFI score, 28 is the cutoff point for Female Sexual Dysfunction (FSD). Furthermore, sexual desire (3.3), sexual arousal (3.4), vaginal lubrication (3.4), orgasm (3.4), sexual satisfaction (3.8), and sexual pain (3.8) are the subdomain cutoff points. Satisfactory sexual function in each domain is indicated by scores above these thresholds. This questionnaire's Persian translation has been validated in Iranian women and has shown good construct validity, internal consistency, and content validity (17).

The participants' psychological well-being was evaluated using the Depression, Anxiety, and Stress Scales-21 (DASS-21). The 21 items in this validated self-report are broken down into three subscales: stress, anxiety, and depression. Each subscale has seven items. On a four-point scale from 0 ("did not apply to me at all") to 3 ("applied to me very much or most of the time"), respondents indicated how much each symptom affected them during the previous week.

The final score for each subscale is multiplied by two to allow comparison with the 42-item version when standard coefficients are used. The score for each subscale is determined by adding the scores of the pertinent items. The following is how symptom severity is interpreted using standard ranges.

Depression: Normal (0–9), Mild (10–13), Moderate (14–20), Severe (21–27), Extremely Severe ≥ 28

Anxiety: Normal (0–7), Mild (8–9), Moderate (10–14), Severe (15–19), Extremely Severe ≥ 20

Stress: Normal (0–14), Mild (15–18), Moderate (19–25), Severe (26–33), Extremely Severe ≥ 34

Extensive psychometric studies have demonstrated that the DASS-21 possesses favorable internal consistency and validity, with Cronbach's alpha reported as 0.93 for the total scale and 0.88, 0.82, and 0.90 for the depression, anxiety, and stress subscales, respectively. The Persian version of this

instrument has also demonstrated acceptable validity and reliability in studies conducted in Iranian clinical and non-clinical populations (18).

Biochemical Assays:

Following a 12-hour overnight fast, blood samples were taken. Fasting blood sugar (FBS), glycated hemoglobin (HbA1c), and two-hour postprandial glucose (2HPP) were measured as biochemical markers of glycemic control. The lipid profile was also assessed, including triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

Delta DP diagnostic kits (Delta Diagnostics, USA) were used for all biochemical analyses. To guarantee accuracy and repeatability of the results, the intra-assay coefficient of variation was kept below 2 percent and the inter-assay coefficient of variation (CV) was kept below 3 percent.

Statistical Analysis:

Only patients who satisfied every requirement of the study protocol were included in the statistical analyses, which were carried out using a per-protocol approach. The database was created and maintained using Excel 2010, and statistical analysis was done using SPSS version 17.0 for Windows. The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. Data were displayed as percentages for categorical variables and as mean $\pm$ standard deviation (SD) or median (interquartile range) for continuous variables, depending on the distribution pattern.

Female sexual function scores were compared using one-way analysis of variance (ANOVA) and independent t-tests. To investigate variable relationships in more detail, mutual information analysis was used. Regardless of whether the relationships are linear or involve second- or third-order interactions, this method quantifies the degree of association between a dependent variable and an independent variable or multiple dependent variables. Therefore, mutual information offers higher accuracy than traditional methods that only identify linear relationships and measure correlation between two variables. The following formula is used to determine the mutual information between two variables, x and y (28).

$$I(x, y) = \sum_x \sum_y P(x, y) \log \left(\frac{p(x, y)}{p(x) p(y)} \right)$$

1

where $P(x, y)$ represents the joint probability distribution of variables x and y , and $P(x)$ and $P(y)$ denote their respective marginal probability distributions.

A confusion matrix that was created by calculating the mutual information between sexual health indices and biochemical variables was presented in order to quantify the relationship between them.

Four algorithms including Random Forest, Gradient Boosting, Lasso, and Ridge were then used separately to conduct pairwise predictive modeling in order to find potential predictive biochemical markers for each sexual health index. The R^2 metric was used to assess each model's predictive power. This analysis identified the particular biochemical marker and the best algorithm that could function as a predictor for each sexual health index.

Results

Table 1 displays the demographic features. The participants' average age was 40.71 ± 6.06 years. The average number of abortions was 0.52 ± 0.93 , and the average number of children was 2.63 ± 1.08 . In terms of employment status, 18.8% of the women were employed, while 81.2% were homemakers. Regarding educational attainment, 5.5 percent were illiterate, 43.5 percent had completed elementary school, 38.6 percent had completed high school, and 12.4 percent had earned a bachelor's degree or above.

In terms of metformin use, 29.5 percent took 500 mg, 46.1 percent took 500–1000 mg, and 24.4 percent took more than 1000 mg. 17.9 percent of participants reported using metformin for 1–5 years, 23.7 percent reported using it for 5–10 years, and 58.4 percent reported using it for more than 10 years. In terms of economic status, 21.3 percent were categorized as low-income, 68.3 percent as middle-income, and 10.4 percent as high-income. Of the participants, 74% had a family history of diabetes, whereas 26% did not.

Table 1
Demographic characteristics of reproductive-aged women with diabetes

Variable	Mean $\pm$ SD (or %)
Age (years)	40.71 $\pm$ 6.06
Number of children	2.63 $\pm$ 1.08
Number of abortions	0.52 $\pm$ 0.93
Occupation – Housewife (%)	81.2%
Occupation – Employed (%)	18.8%
Education – Illiterate (%)	5.5%
Education – Primary school (%)	43.5%
Education – High school diploma (%)	38.6%
Education – bachelor's degree and higher (%)	12.4%
Metformin dosage – 500 mg (%)	29.5%
Metformin dosage – 500–1000 mg (%)	46.1%
Metformin dosage – >1000 mg (%)	24.4%
Duration of metformin use – 1–5 years (%)	17.9%
Duration of metformin use – 5–10 years (%)	23.7%
Duration of metformin use – >10 years (%)	58.4%
Economic status – Poor (%)	21.3%
Economic status – Average (%)	68.3%
Economic status – Wealthy (%)	10.4%
Family history of diabetes – Yes (%)	74.0%
Family history of diabetes – No (%)	26.0%

Table 2 presents the biochemical parameters of the study population. The mean levels of fasting blood glucose (FBS), glycated hemoglobin (HbA1c), and two-hour postprandial glucose (2HPP) indicated inadequate glycemic control in a considerable proportion of participants. Dyslipidemia was also prevalent, with many patients exhibiting elevated triglycerides and LDL-C levels, along with reduced HDL-C concentrations.

Table 2
Biochemical parameters of reproductive-aged women
with diabetes

Parameter	Mean $\pm$ SD
Fasting blood glucose (mg/dL)	153.6 $\pm$ 50.8
HbA1c (%)	7.7 $\pm$ 1.7
2-hour postprandial glucose (mg/dL)	218.7 $\pm$ 72.3
Total cholesterol (mg/dL)	187.6 $\pm$ 42.6
Triglycerides (mg/dL)	174.5 $\pm$ 67.1
HDL-C (mg/dL)	51.2 $\pm$ 13.3
LDL-C (mg/dL)	100.6 $\pm$ 28.7
VLDL (mg/dL)	33.4 $\pm$ 14.5

The distribution of biochemical markers among female diabetics between the ages of 18 and 45 is shown in Fig. 1. HbA1c, FBS, and 2-hour postprandial glucose (2HPP) are among the glucose indices. Total cholesterol, triglycerides, HDL-C, LDL-C, and VLDL are all included in lipid profiles. For glucose and lipid markers, the reported units are usually mg/dL; for HbA1c, they are in percentages.

In Fig. 2 the distribution of scores for the subscales of the Female Sexual Function Index (FSFI) including sexual desire, arousal, vaginal lubrication, orgasm, sexual satisfaction, and pain along with overall FSFI scores in women with diabetes is illustrated. Separate histograms also depict the distribution of scores on the Depression, Anxiety, and Stress Scale (DASS-21), the total DASS score, as well as variables related to quality of life and marital satisfaction.

According to FSFI criteria, a total score of ≤ 28 is indicative of female sexual dysfunction (FSD). The clinical cut-off values for the subscales are as follows: desire 3.3, arousal 3.4, lubrication 3.4, orgasm 3.4, satisfaction 3.8, and pain 3.8. Scores above these thresholds reflect optimal sexual functioning. Examination of the score distributions shows that most women with diabetes scored below the clinical cut-off values for the total FSFI score and most subscales, indicating a high prevalence of sexual dysfunction and reduced sexual performance in this population. This pattern is particularly pronounced in the domains of desire, arousal, and sexual pain.

For mental health, the DASS-21 subscale scores are interpreted based on standard severity ranges, with higher values indicating greater levels of depression, anxiety, and stress. The distribution reveals that a considerable proportion of participants fall within the moderate to severe ranges across all three subscales, suggesting a substantial psychological burden among women with diabetes. The concurrence of lower FSFI scores with higher DASS-21 scores analytically reflects an overlap between impaired sexual function and poor psychological status in this population.

Figure 3 illustrates the distribution of scores across the six domains of the Female Sexual Function Index (FSFI) sexual desire, arousal, vaginal lubrication, orgasm, sexual satisfaction, and pain among women with diabetes (n = 124). The dashed blue and green vertical lines represent the mean and median scores, respectively, while the dashed red vertical line indicates the clinical cutoff point for each subscale.

According to the FSFI scoring system, the total score is calculated by summing the weighted scores of the six domains (range: 2–36), with higher scores indicating better sexual function. The cutoff points applied in this study include a total FSFI score of 28 and domain-specific thresholds of 3.3 for sexual desire; 4.3 for arousal, lubrication, and orgasm; and 3.8 for sexual satisfaction and pain.

Analysis of the score distributions indicates that, in most subscales, a substantial proportion of women with diabetes scored below the clinical cutoff points. The clustering of both mean and median scores below or close to these thresholds suggests a high prevalence of sexual dysfunction and the absence of optimal sexual functioning within this population. This pattern indicates that sexual dysfunction among women with diabetes is common, multidimensional, and heterogeneous, affecting different aspects of sexual function to varying degrees.

Figure 4 presents boxplots of metabolic indicators including fasting blood sugar (FBS), two-hour postprandial glucose (2HPP), glycated hemoglobin (HbA1c), triglycerides, total cholesterol, HDL, LDL, and VLDL, along with measures of female sexual function (FSFI), mental health (DASS-21), sexual quality of life (SQOL-F), and marital satisfaction in women with diabetes. The central line within each box represents the median, the box boundaries indicate the first and third quartiles, and points beyond the whiskers represent outliers.

Regarding metabolic indicators, the relatively wide dispersion and the presence of outliers particularly in FBS, 2HPP, HbA1c, and lipid profiles suggest suboptimal metabolic control in a considerable proportion of participants. The median HbA1c values appear to be concentrated above clinically recommended levels, indicating inadequate glycemic control in this population, which may play a significant role in the development of both physical and sexual complications.

In the domain of sexual function, the boxplots of the FSFI subscales and the total FSFI score demonstrate that the median scores in most domains fall below the clinical cutoff points. This pattern is particularly pronounced in the domains of sexual desire, arousal, lubrication, and sexual pain, supporting the high prevalence of female sexual dysfunction (FSD) among women with diabetes. Moreover, the total FSFI score in a large proportion of the sample falls below the threshold value of 28, indicating suboptimal sexual functioning in this population.

In terms of mental health, the median scores for depression, anxiety, and stress, as well as the total DASS score, fall within the mild to moderate ranges. The presence of extreme values in some participants suggests a considerable psychological burden among certain subgroups of women with diabetes. The co-occurrence of lower FSFI scores with higher DASS-21 scores further reflects a pattern of comorbidity between sexual dysfunction and psychological distress.

Investigating the Relationship Between Biochemical Variables and Sexual Health Indices

Machine learning tools were used in this study to investigate the association between biochemical variables and sexual health indices, as previously described. An entropy-based tool called Mutual Information (MI) evaluates this relationship regardless of whether it is linear or non-linear. Figure 5 displays the confusion matrix that was obtained from this measurement.

When compared to other biochemical parameters, some biochemical indicators, like triglycerides, show stronger information overlap (associative relationships) with indicators related to sexual health, such as sexual pain, stress, and depression, as shown in Fig. 5. Triglycerides and VLDL show the strongest degree of information sharing with sexual health indicators among the biochemical variables.

Four machine learning algorithms—Random Forest (RF), Gradient Boosting Regression (GBR), Lasso Regression, and Ridge Regression—were used to determine which biochemical variables could function as predictors for each sexual health index. For each pair of biochemical variables and sexual health indices (a total of $12 \times 4 = 48$ combinations), the R^2 score was computed. The best-performing predictive model and its matching R^2 value for each of the 12 main sexual health indices are listed in Table 3, which summarizes the findings. It should be noted when interpreting these results that values above 0.5 indicate that the model is an effective predictor, whereas values between 0.3 and 0.5 typically indicate a moderate predictive model. For example, none of the used algorithms were successful in predicting the Desire index, but the GBR algorithm showed good predictive performance for the Pain index.

Table 3

Predictive performance ($\backslash \text{varvec}R^2$ values) of selected algorithms for sexual health indices, utilizing glycemic variables variables. Shown are the $\backslash \text{varvec}R^2$ values for the best predictive model identified for each index

Target	Best_model	R^2
Desire	Lasso	0.071079
Arousal	GBR	0.423233
Lubrication	GBR	0.239816
Orgasm	GBR	0.312764
Satisfaction	RF	-0.15187
Pain	GBR	0.841072
Total_FSKI	RF	0.297261
Sexual_Quality_of_Life	RF	0.381681
Depression	RF	0.428932
Anxiety	RF	0.144313
Stress	RF	0.483095
Total_DASS	RF	0.471679

Table 4. Predictive performance ($\backslash \text{varvec}R^2$ values) of selected algorithms for sexual health indices, utilizing lipid variables. Shown are the $\backslash \text{varvec}R^2$ values for the best predictive model identified for each index.

The relationships between specific glycemic/lipid variables and sexual health indices using the best predictive algorithm are also shown in Figs. 6 and 7.

Figure 6 presents the results of correlation analysis and predictive modeling examining the relationships between glycemic indicators and different domains of mental health and sexual function among women with diabetes. Two-hour postprandial blood glucose (2HPP) was identified as the most important variable in predicting the total Female Sexual Function Index (Total FSFI) score. The standardized coefficients derived from the LASSO regression model indicate that HbA1c exerts the strongest negative effect on the sexual desire domain. In addition, the results of the Gradient Boosting Regression (GBR) model highlight the dominant role of 2HPP in predicting the domains of sexual arousal and vaginal lubrication.

In the prediction of orgasm using the GBR model, two-hour postprandial glucose (2HPP) shows the highest importance, followed by fasting blood sugar (FBS) and HbA1c. For the pain domain, HbA1c emerges as the most important predictor, while 2HPP and FBS demonstrate lower levels of importance. In predicting sexual satisfaction using the Random Forest (RF) model, 2HPP again appears as the most influential indicator, with FBS and HbA1c ranking subsequently. Overall, these findings suggest that postprandial glucose fluctuations (2HPP) play a key role in most aspects of sexual function among women with diabetes, whereas long-term glycemic control (HbA1c) appears to be more strongly associated with the pain domain.

Postprandial glucose responses (2HPP) have a significant predictive role in mental health, with the highest importance weights for stress, anxiety, and depression, according to data mining analysis of Fig. 6. In the meantime, FBS had a complementary role in certain subsets, and HbA1c, an indicator of chronic glycemic control, showed a significant impact across all domains. In particular, elevated 2HPP and HbA1c are linked to higher scores for anxiety and stress disorders, indicating that chronic glycemic control and a quick post-meal blood glucose response may worsen anxiety and stress behaviors, possibly by interfering with neuro-hormonal axes. In terms of depression, HbA1c has a significant impact and 2HPP has the highest predictive weight, suggesting a connection between the severity of depression and post-meal glucose fluctuations and long-term glycemic control.

Figure 7 illustrates the outcomes of both correlational analysis and predictive modeling investigating the links between lipid parameters and diverse facets of sexual function and mental health in the female diabetic population

FSFI data and lipid biochemical indicators including triglycerides, HDL, LDL, VLDL, total cholesterol, and the LDHD index were collected, and variable importance was analyzed using Random Forest, LASSO, and Gradient Boosting Regressor (GBR) models. The results indicated that triglycerides played the most prominent role in explaining overall sexual health (Total FSFI), followed by HDL and total cholesterol.

At the domain level, sexual desire and arousal demonstrated the strongest associations with triglycerides and HDL. The domains of pain and orgasm were primarily influenced by triglycerides and LDL, whereas sexual satisfaction was associated with a combination of HDL and VLDL. Correlation analysis further revealed that higher triglyceride levels were associated with reductions in several FSFI domains, while HDL showed a positive association with sexual function.

The data mining analysis of Fig. 7 also indicates that lipid indices play a significant role in predicting psychosocial dimensions including stress, anxiety, and depression. For stress, LDL, Cholesterol, and VLDL had the highest weights in the GBR Stress plot, and lower values of Triglycerides or a higher ratio of HDL to other indices correlated with lower stress severity, suggesting the impact of metabolic status on physiological and chronic stress responses. In anxiety, HDL had the highest importance, followed by LDHD and LDL, while Triglycerides and Cholesterol showed a moderate effect; these findings indicate that the balance of plasma lipids and the metabolic profile can be associated with anxiety severity. For depression, Triglycerides and LDL appeared with high weights, and Cholesterol and VLDL also played

important roles, while HDL was relatively less but still effective, suggesting a combined effect of plasma lipids on depression severity. These patterns demonstrate that lipid indices, particularly LDL, Triglycerides, VLDL, and HDL, act as significant predictors of mental health and, along with glycemic indices, reflect metabolic status and neuropsychological function

Discussion

The findings of the present study indicate that female sexual dysfunction (FSD) is highly prevalent among women with diabetes and affects multiple domains of sexual function simultaneously. Based on the distribution of Female Sexual Function Index (FSFI) scores presented in Figs. 2 and 3, most participants obtained scores below the clinical cutoff points for both the total FSFI score and most of the subscales, indicating suboptimal sexual functioning in this population. This pattern was particularly pronounced in the domains of sexual desire, arousal, vaginal lubrication, and sexual pain, supporting the multidimensional and heterogeneous nature of sexual dysfunction among women with diabetes.

These findings are consistent with results reported in previous studies. Rosen et al., who originally introduced the FSFI instrument, reported that concurrent reductions across multiple subscales represent a key characteristic of sexual dysfunction in women with chronic conditions, including diabetes (19). Similarly, Sansone and colleagues found that women with type 2 diabetes had significantly lower scores in sexual desire, arousal, and sexual satisfaction compared with healthy controls (20). Furthermore, a meta-analysis conducted by Pontiroli et al. demonstrated that the prevalence of FSD among women with diabetes is substantially higher than in the general population and often involves more than one domain of sexual functioning (21).

Diabetes-induced female sexual dysfunction (FSD) arises from a synergistic interplay between vascular hemodynamic compromise and peripheral neuropathy. Chronic hyperglycemia, coupled with diminished paraoxonase-1 (PON-1) activity, precipitates systemic oxidative stress and endothelial dysfunction, thereby impairing genital blood flow and nitric oxide-mediated vasorelaxation. This pathophysiological decline is further exacerbated by neuroendocrine disruptions within the hypothalamic-pituitary-ovarian axis and reduced nitric oxide bioavailability, culminating in clinical manifestations such as vaginal sicca and attenuated clitoral responsiveness. Ultimately, the convergence of these metabolic disturbances with psychological stressors underscores a multifactorial clinical landscape, necessitating an integrated, multidisciplinary approach to therapeutic intervention(22).

From a mental health perspective, the findings presented in Figs. 2 and 4 indicate that a considerable proportion of women with diabetes fall within the moderate to severe ranges of depression, anxiety, and stress based on the DASS-21 scale. The co-occurrence of lower FSFI scores with higher DASS-21 scores suggests a significant overlap between sexual dysfunction and adverse psychological status in this population. Numerous studies have emphasized the role of psychological factors as strong predictors of female sexual dysfunction. **A systematic review and meta-analysis** reported that depression and anxiety are not only consequences of sexual dysfunction but may also function as exacerbating factors (23).

Among women with diabetes, this relationship may be even more complex, as psychological stress related to living with a chronic illness, fear of complications, and reduced quality of life may indirectly impair sexual functioning. Findings from a study by Winkley et al. indicated that the severity of depression is significantly correlated with reduced sexual desire and satisfaction in diabetic patients (24). In Iran, validation studies using the Persian versions of the FSFI and DASS-21 have similarly demonstrated that psychological disorders play an important role in the reduction of sexual function among women with diabetes (25, 26).

In addition to psychological factors, the findings presented in Fig. 4 indicate suboptimal metabolic control in a considerable proportion of the study sample. The concentration of median HbA1c values above recommended clinical levels (Glycated hemoglobin (HbA1c) $\geq 6.5\%$), together with the wide dispersion observed in glycemic and lipid indicators, reflects inadequate metabolic regulation in this population. Existing evidence suggests that chronic hyperglycemia, through mechanisms such as endothelial dysfunction, peripheral neuropathy, and reduced pelvic blood flow, can directly impair sexual arousal, vaginal lubrication, and orgasmic function (24). In this regard, Rutherford and colleagues reported that higher HbA1c levels are independently associated with lower FSFI scores among women with diabetes (27).

Overall, the findings of the present study are consistent with the existing literature and indicate that female sexual dysfunction in women with diabetes is a multifactorial phenomenon resulting from a complex interaction of metabolic, psychological, and social factors. The concurrent presence of lower FSFI scores, higher DASS-21 scores, and poor glycemic control highlights the need for comprehensive and multidimensional approaches in clinical assessment and intervention aimed at improving sexual health and overall quality of life in women with diabetes.

Glycemic Indicators and Sexual Function

The findings presented in Fig. 6 indicated that 2HPP was the most important predictive variable for the total FSFI score and for most domains of sexual function, particularly arousal, lubrication, orgasm, and sexual satisfaction. This result is consistent with studies showing that postprandial glucose fluctuations exert more detrimental effects on vascular function, endothelial integrity, and peripheral neural responses compared with FBS or HbA1c (28). Because female sexual function is directly dependent on adequate pelvic blood flow, autonomic nerve activity, and hormonal regulation, elevated 2HPP may reduce arousal and vaginal lubrication through mechanisms involving oxidative stress and disruption of the nitric oxide pathway (29).

It is also explained that HbA1c, as an indicator of long-term glycemic control, had the strongest negative influence on sexual desire and the pain domain. This finding is consistent with evidence suggesting that chronic hyperglycemia may exacerbate pain perception and reduce sexual desire through mechanisms such as diabetic neuropathy, diminished nerve sensitivity, and chronic inflammatory changes (29). Some studies have reported a weaker association between HbA1c and different dimensions of sexual function

(30) however, differences in study design, study populations, and the use of nonlinear modeling approaches in the present study may help explain this discrepancy.

Lipid Indicators and Sexual Function:

The results presented in Fig. 7 showed that triglycerides were the most influential factor in predicting the total FSFI score and several domains of sexual function. Elevated triglyceride levels were associated with reduced sexual desire and arousal, as well as increased sexual pain, whereas HDL demonstrated a protective effect. These findings are consistent with epidemiological studies that have identified dyslipidemia as one of the major risk factors for sexual dysfunction among women with diabetes (29, 30). Esposito et al established that hyperlipidemia significantly impairs female sexual function across the FSFI domains of desire, arousal, lubrication, and orgasm compared to normolipidemic controls. These findings highlight the critical role of lipid dysregulation in the pathogenesis of sexual dysfunction, likely through compromised vascular integrity and systemic metabolic stress. Consequently, optimizing serum lipid profiles and implementing aggressive preventive strategies represent essential therapeutic avenues for the preservation and restoration of sexual health in this population(31).

Conversely, the beneficial role of HDL in sexual satisfaction and desire may be explained by its anti-inflammatory properties, its ability to improve vascular function, and its role in reducing oxidative stress (32).The differing relative importance of LDL and VLDL across various FSFI domains also suggests that the effects of lipid indicators on sexual function are not uniform but rather depend on the complex interaction between lipid metabolism, inflammatory status, and neural regulation (33).

Glycemic Indicators and Mental Health:

The findings presented in Fig. 6 (glycemic indicators) showed that 2HPP was the strongest predictor of stress, anxiety, and depression, while HbA1c also demonstrated a substantial effect across all domains. These results are consistent with evidence linking acute glucose fluctuations to activation of the hypothalamic–pituitary–adrenal (HPA) axis, increased cortisol secretion, and exacerbation of anxiety and depressive symptoms (34).Postprandial hyperglycemia may lead to mood instability, mental fatigue, and heightened sensitivity to stress, whereas chronic hyperglycemia, reflected by elevated HbA1c levels, may contribute to more persistent depressive states through mechanisms involving systemic inflammation and alterations in neurotransmitter regulation (35).

Uncontrolled diabetes may precipitate neuroinflammatory brain alterations and neurotransmitter dysregulation, potentially predisposing patients to mood disorders (36, 37) However, empirical evidence remains divergent; while poor glycemic control is frequently associated with increased psychological distress (38), integrated multidisciplinary care models have demonstrated the ability to achieve optimal HbA1c targets regardless of comorbid psychiatric status (39).

Data-driven analysis in Fig. 7 revealed that LDL, triglycerides, and VLDL played prominent roles in predicting stress and depression, whereas HDL showed the greatest importance in relation to anxiety. These findings are consistent with studies reporting an association between dyslipidemia and mood as

well as anxiety disorders (40, 41). Plasma lipids may influence mental health through their effects on neuronal membrane structure, neurotransmitter function, and inflammatory pathways (42). The protective role of HDL in anxiety is also likely related to its anti-inflammatory properties and its regulatory effects on the HPA axis.

Recent evidence indicates that LDL-C significantly modifies the association between triglycerides and depression, a process potentially mediated by sequential neuroinflammatory mechanisms. High LDL-C levels are thought to compromise the blood–brain barrier, allowing TG-derived free fatty acids to enter the central nervous system and activate microglial Toll-like receptor 4, thereby triggering inflammatory cascades that exacerbate depressive symptoms. Moreover, the cumulative load of apolipoprotein B-containing lipoproteins, reflected in elevated LDL-C and TG-rich particles, contributes to systemic low-grade inflammation and endothelial dysfunction, further predisposing individuals to neurovascular impairment (43).

Mutual Information Analysis Between Biochemical Indicators and Psychosexual Health

The mutual information matrix (Fig. 5) indicated that triglycerides and VLDL had the greatest informational overlap with indicators of sexual pain, stress, and depression. This finding highlights the importance of dyslipidemia as a common contributing factor linking metabolic, psychological, and sexual dysfunction. Such a pattern of results is consistent with integrated biological models that conceptualize diabetes not merely as a metabolic disorder but as a multisystem condition with significant psychosexual consequences (44).

Conclusion

Overall, the results of the present study suggest that postprandial metabolic responses (2HPP) and dyslipidemia particularly elevated triglyceride levels play key roles in explaining disturbances in sexual and mental health among women with diabetes. The application of data-driven modeling approaches made it possible to identify nonlinear patterns and complex interactions among variables, indicating that classical metabolic indicators alone may not fully capture the broader consequences of diabetes. These findings underscore the importance of targeted therapeutic strategies aimed at controlling postprandial glucose fluctuations and improving lipid profiles as effective approaches for enhancing both sexual and psychological health in women with diabetes.

Declarations

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Author Contribution

"N.T. and F.M. wrote the main manuscript text and M.A. prepared figures . All authors reviewed the manuscript."

Data Availability

Data presented in this study are available on request from the corresponding authors.

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Tables

Table 4 is not available with this version.

Figures

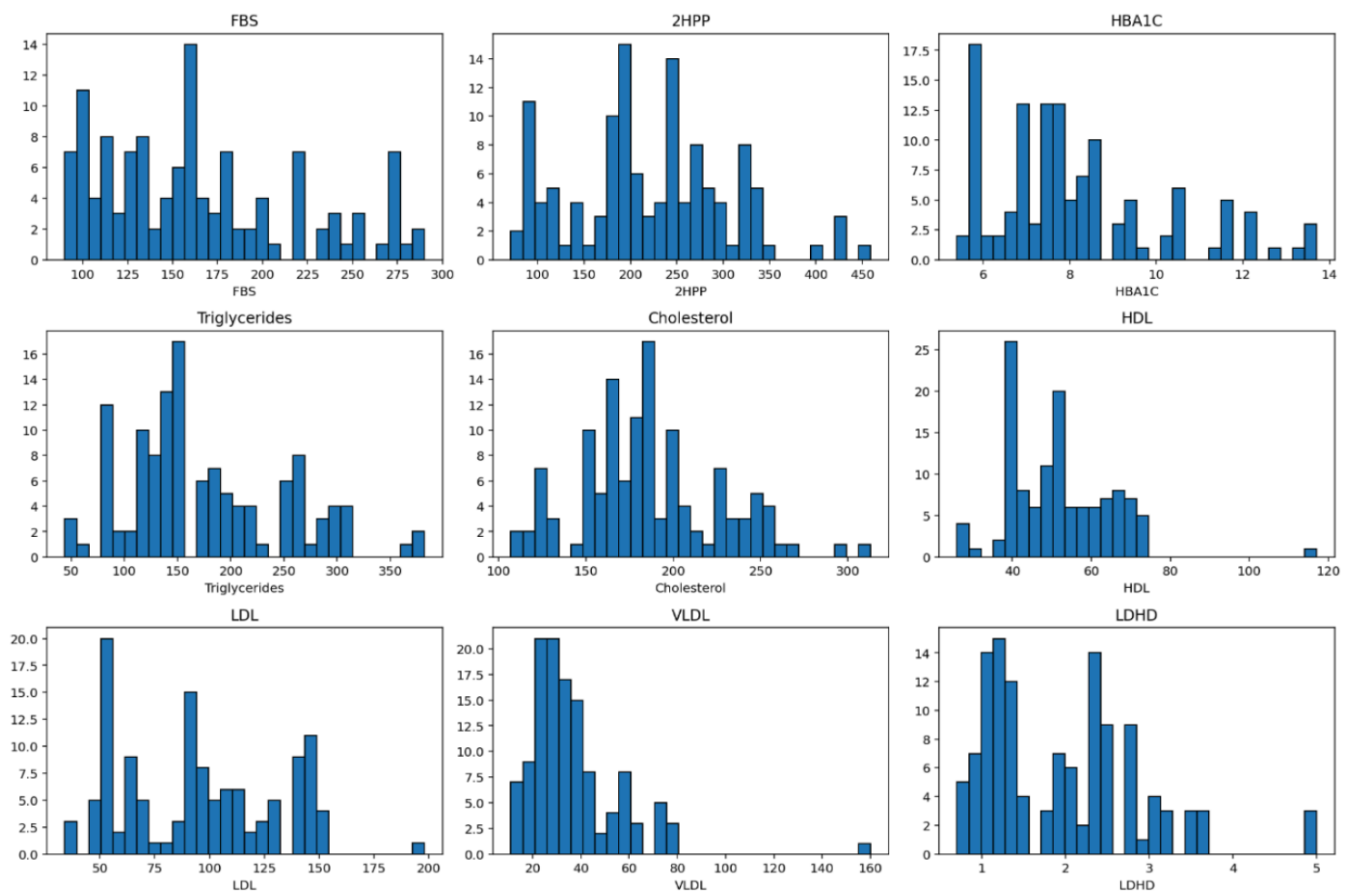


Figure 1

Distribution of biochemical values in reproductive-aged women with diabetes (18– 45 years)

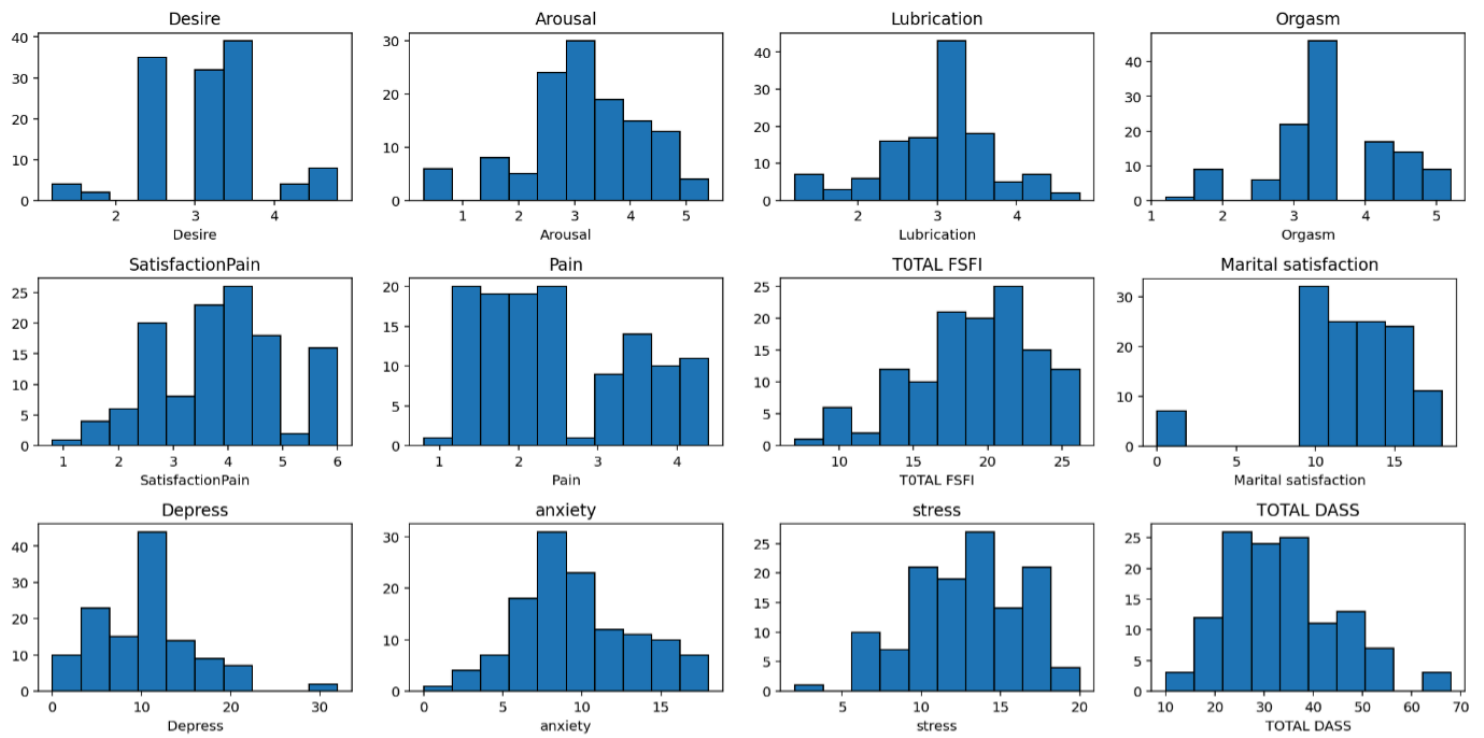


Figure 2

Distribution of sexual function (FSFI), mental health (DASS-21), and related variables in women with diabetes

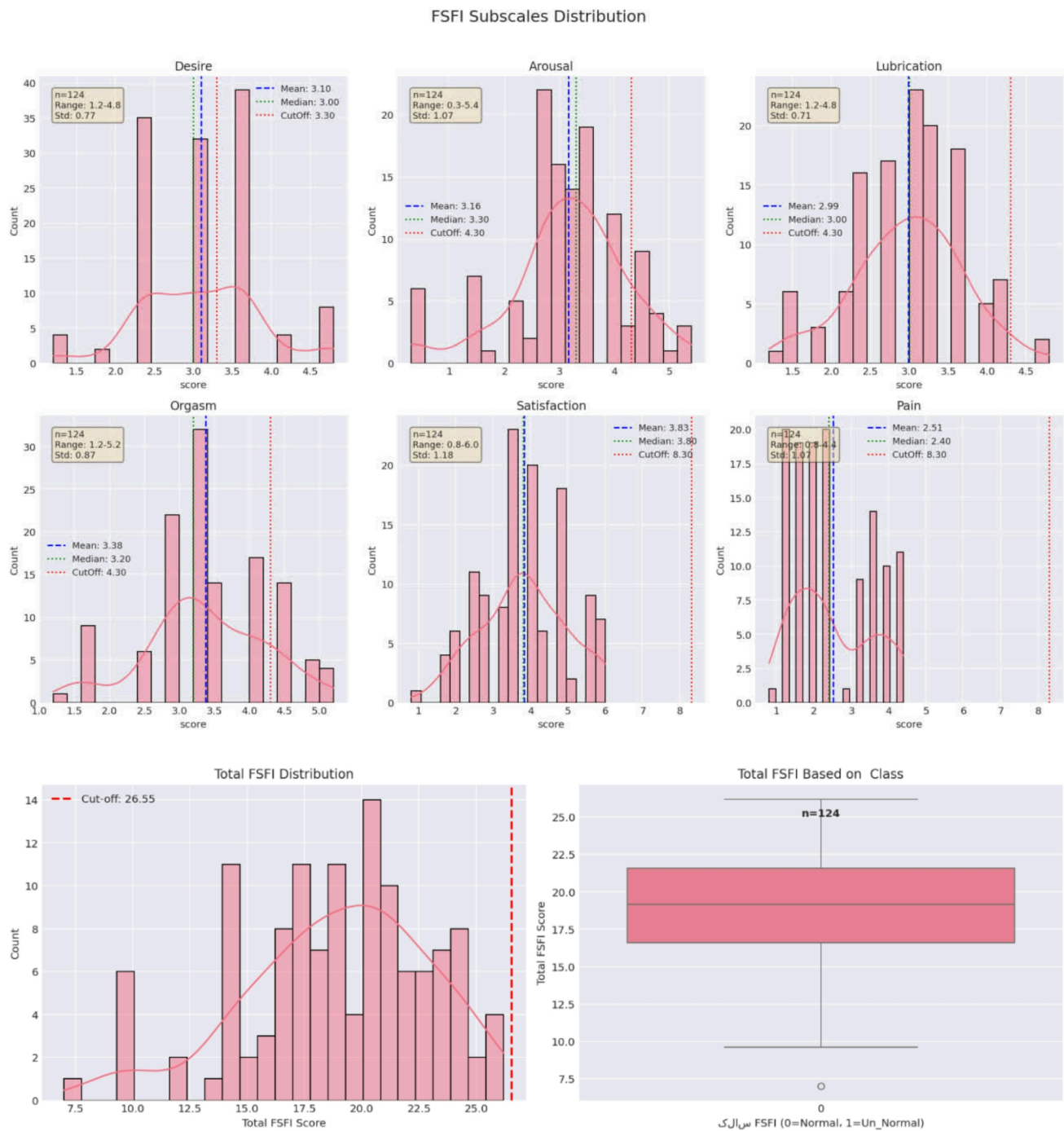


Figure 3

Distribution of Female Sexual Function Index (FSFI) Domain Scores and Comparison with Clinical Cutoff Points

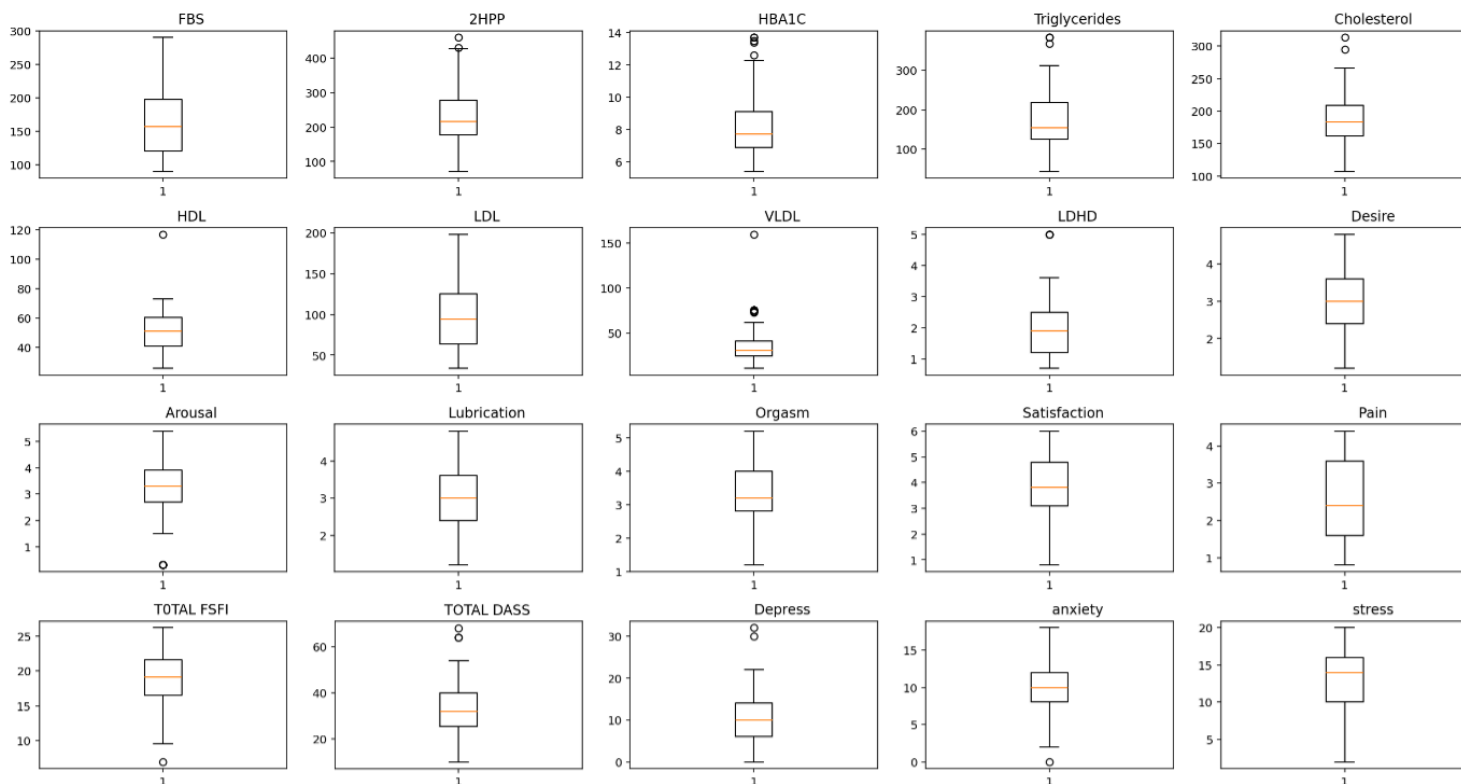


Figure 4

Boxplots of Metabolic Indicators, Sexual Function, Mental Health, and Related Variables in Women with Diabetes

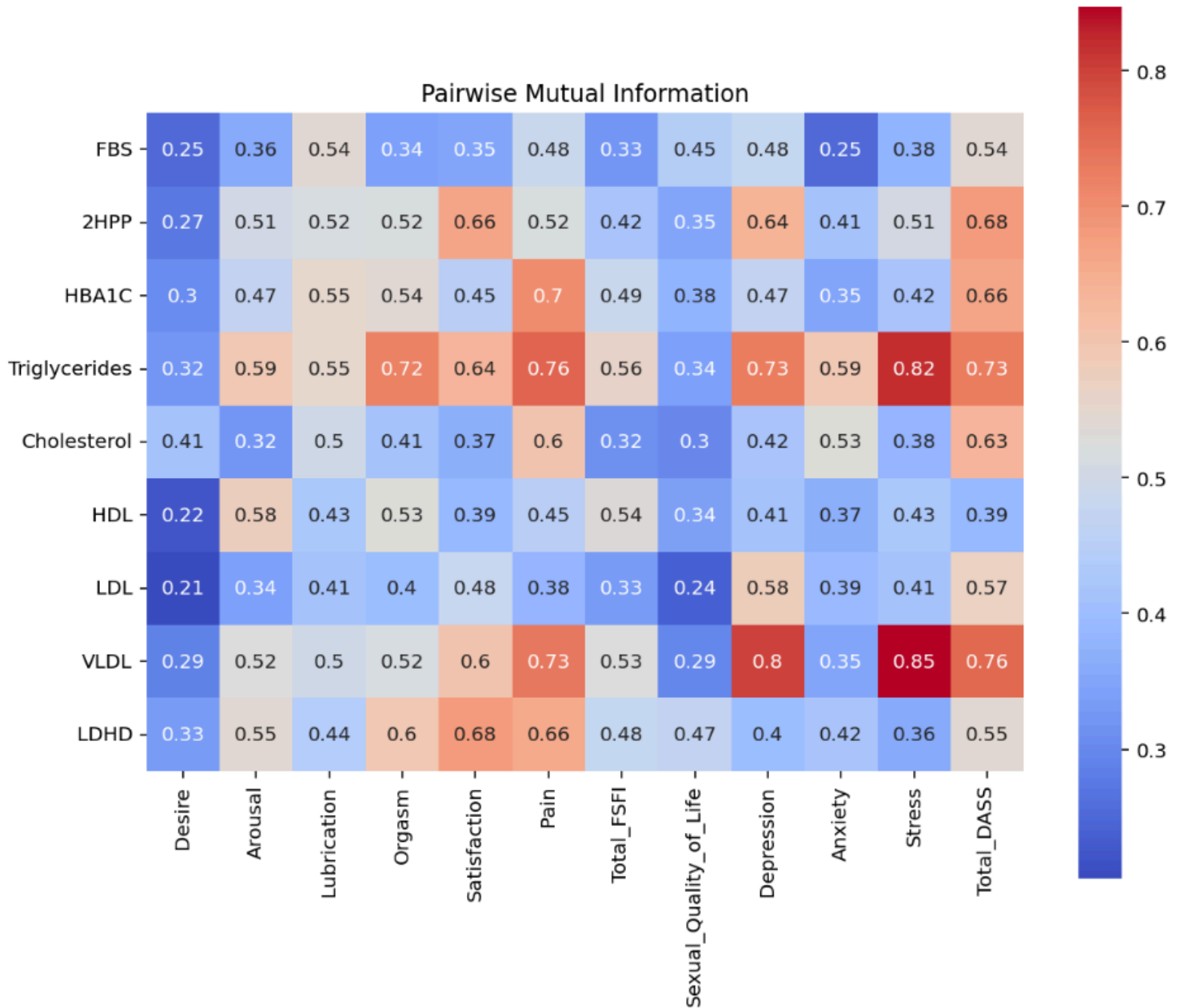


Figure 5

Confusion (Information-Sharing) Matrix Between Biochemical Variables and Sexual Health Indicators

Best Model for Each Target



Figure 6

Visualization of the relationship between glycemic biochemical variables and sexual and mental health indices using the best predictive algorithm.

Best Model for Each Target

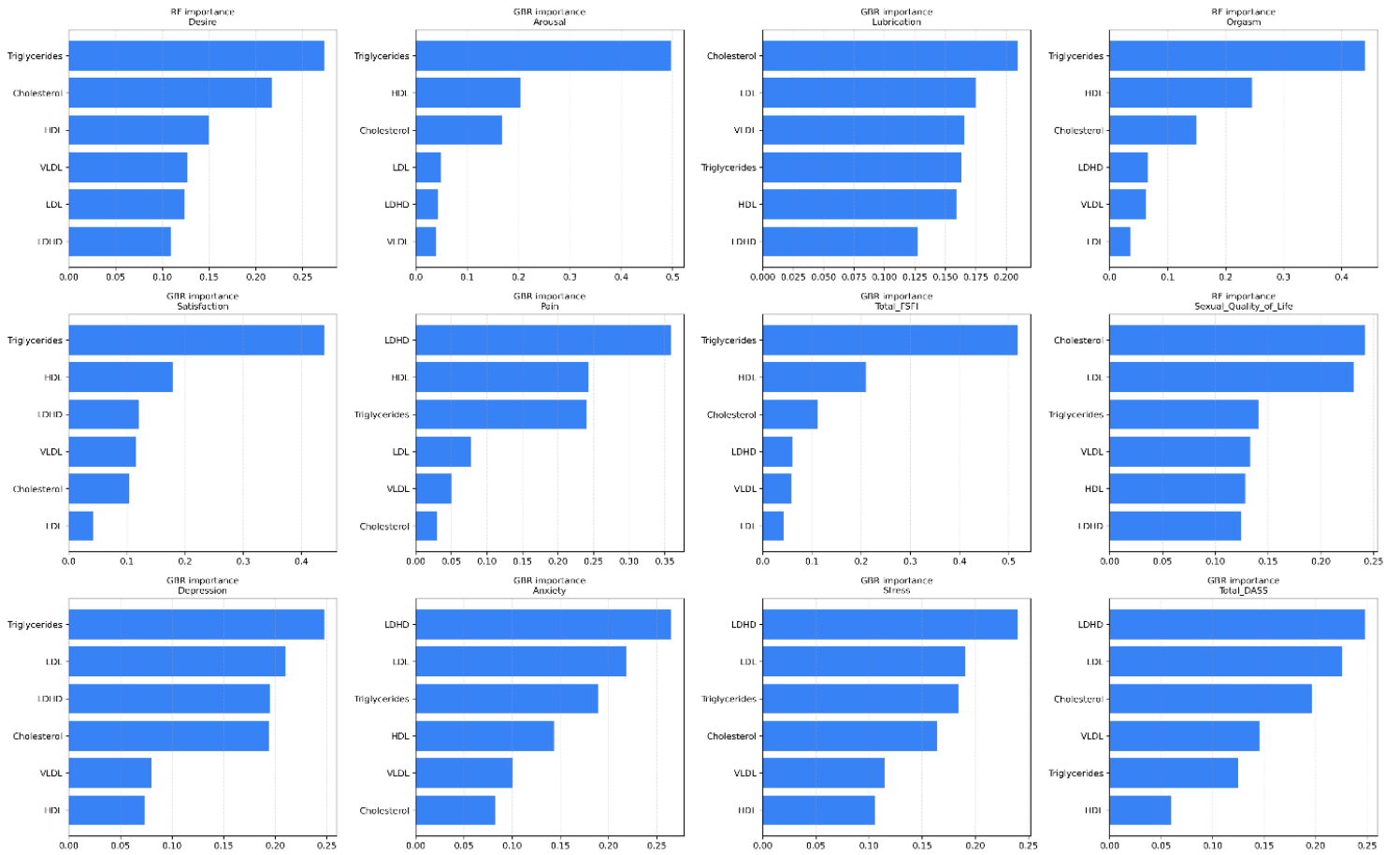


Figure 7

Visualization of the relationship between lipid biochemical variables and sexual and mental health indices using the best predictive algorithm.