

**VICTOR BABEȘ UNIVERSITY OF MEDICINE
AND PHARMACY TIMIȘOARA
FACULTY OF MEDICINE
DEPARTMENT VII – INTERNAL MEDICINE II**

BORȚUN ANA-MARIA CRISTINA



PhD THESIS

**UNRAVELING THE COMPLEXITIES OF SEXUAL FUNCTION
IN YOUNG WOMEN:
A MULTI-DIMENSIONAL INVESTIGATION OF
PHYSIOLOGICAL AND PATHOLOGICAL HORMONAL
MODELS, AND ORGANIC, EMOTIONAL, AND
PSYCHOLOGICAL FACTORS**

A B S T R A C T

Scientific Coordinator

PROF. UNIV. DR. STOIAN DANA

**Timișoara
2023**

TABLE OF CONTENTS

| | |
|---|------|
| List of publications | VII |
| List of abbreviations..... | VIII |
| List of figures | X |
| List of tables..... | XI |
| Acknowledgements..... | XIV |
| INTRODUCTION | XV |
| GENERAL PART | 1 |
| 1. PHYSIOLOGY OF THE FEMALE SEXUAL RESPONSE | 1 |
| 1.1. The female sexual response cycle | 1 |
| 1.1.1. The Masters and Johnson model | 2 |
| 1.1.2. The Kaplan model..... | 5 |
| 1.1.3. The Basson model..... | 8 |
| 1.1.4. The Bancroft and Janssen dual control model | 10 |
| 1.1.5. Women's endorsement of sexual response models | 12 |
| 1.2. Factors influencing female sexuality..... | 13 |
| 1.2.1. Biological factors..... | 13 |
| 1.2.2. Psychological and emotional factors | 15 |
| 1.2.3. Social and interpersonal factors | 16 |
| 1.3. Female sexual response cycle as a neuroendocrine process | 18 |
| 2. THE ROLE OF HORMONES IN NORMAL FEMALE SEXUALITY | 22 |
| 2.1. The sex hormones | 22 |
| 2.1.1. Estradiol and other estrogens..... | 22 |
| 2.1.2. Testosterone and other androgens..... | 23 |
| 2.1.3. Progesterone | 25 |
| 2.2. The pituitary hormones | 26 |
| 2.2.1. Luteinizing hormone | 26 |
| 2.2.2. Follicle-stimulating hormone | 27 |
| 2.2.3. Prolactin..... | 28 |
| 2.2.4. Oxytocin | 29 |

| | |
|---|----|
| 3. THE MAIN HORMONAL ENTITIES IMPACTING FEMALE SEXUAL FUNCTION | 31 |
| 3.1. Hyperprolactinemia | 31 |
| 3.2. Menopause and ovarian insufficiency..... | 32 |
| 3.3. Particular situations | 33 |
| 3.3.1. Thyroid autoimmune disease..... | 33 |
| 3.3.2. Polycystic ovary syndrome | 36 |
| 4. THE HORMONAL MODEL OF PREGNANCY AND ITS INFLUENCE ON FEMALE SEXUALITY | 38 |
| 4.1. Overview of hormonal changes during pregnancy | 38 |
| 4.2. The evolution of female sexual function during pregnancy..... | 39 |
| 4.2.1. Female sexuality in the first trimester of pregnancy | 39 |
| 4.2.2. Female sexuality in the second trimester of pregnancy..... | 39 |
| 4.2.3. Female sexuality in the third trimester of pregnancy | 40 |
| 4.3. Hormonal effects on sexual functioning during pregnancy..... | 40 |
| SPECIFIC PART..... | 43 |
| 5. GENERAL OBJECTIVES | 43 |
| 6. PRELIMINARY STUDY: PSYCHOMETRIC VALIDATION OF THE ROMANIAN VERSION OF THE FEMALE SEXUAL FUNCTION INDEX (FSFI-RO) | 45 |
| 6.1. Background and aims of the research | 45 |
| 6.2. Materials and methods | 47 |
| 6.2.1. Subjects | 47 |
| 6.2.2. Instruments and procedure..... | 47 |
| 6.2.3. Statistical analysis | 49 |
| 6.3. Results..... | 51 |
| 6.4. Discussion | 53 |
| 6.5. Conclusions | 57 |
| 7. STUDY I: THYROID AUTOIMMUNE DISEASE – IMPACT ON SEXUAL FUNCTION IN YOUNG WOMEN | 58 |
| 7.1. Aims of the research..... | 58 |
| 7.2. Materials and methods | 58 |
| 7.2.1. Subjects | 58 |

| | |
|---|------|
| 7.2.2. Clinical and paraclinical evaluation | 59 |
| 7.2.3. Psychometric evaluation | 60 |
| 7.2.4. Statistical analysis | 61 |
| 7.3. Results | 62 |
| 7.4. Discussion | 65 |
| 7.5. Conclusions | 68 |
| 8. STUDY II: EFFECTS OF HORMONAL PROFILE, WEIGHT, AND BODY IMAGE ON SEXUAL FUNCTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME | 69 |
| 8.1. Aims of the research | 69 |
| 8.2. Materials and methods | 69 |
| 8.2.1. Subjects | 69 |
| 8.2.2. Clinical and paraclinical evaluation | 70 |
| 8.2.3. Psychometric evaluation | 72 |
| 8.2.4. Statistical analysis | 72 |
| 8.3. Results | 73 |
| 8.4. Discussion | 76 |
| 8.5. Conclusions | 79 |
| 9. STUDY III: THE PARADOX OF SEXUAL DYSFUNCTION OBSERVED DURING PREGNANCY | 80 |
| 9.1. Aims of the research | 80 |
| 9.2. Materials and methods | 80 |
| 9.2.1. Subjects | 80 |
| 9.2.2. Instruments and procedure | 81 |
| 9.2.3. Statistical analysis | 84 |
| 9.3. Results | 84 |
| 9.4. Discussion | 89 |
| 9.5. Conclusions | 96 |
| FINAL CONCLUSIONS | 98 |
| REFERENCES | 102 |
| ANNEX I. | I |
| IN EXTENSO PUBLICATIONS | XXVI |

GENERAL PART

A comprehensive investigation of physiological and pathological hormonal models is critical to understanding young women's sexual function. Hormones play a vital role in regulating sexual desire, arousal, and satisfaction. Studying the intricate hormonal mechanisms at play during this stage of life can offer valuable insights into the physiological underpinnings of sexual function. Furthermore, uncovering potential hormonal dysregulations or pathologies can guide the development of targeted interventions for young women experiencing sexual difficulties.

Emotional and psychological factors significantly influence sexual function and satisfaction. Young women face unique emotional and psychological challenges, such as body image concerns, self-esteem issues, and relationship dynamics, which can impact their sexual experiences. Investigating the emotional and psychological aspects of sexual function in this population can enhance our understanding of the interplay between mental well-being and sexual health. It can also inform interventions that address emotional and psychological factors to promote healthy sexual development and positive sexual experiences.

Body composition can affect sexual function and body image perception. Young women often experience body dissatisfaction, which can have a significant impact on their sexual well-being. Understanding the relationship between body composition factors and sexual function can provide insights into the mechanisms underlying these associations. This knowledge can guide interventions aimed at promoting body acceptance and enhancing sexual satisfaction among young women.

SPECIFIC PART

1. GENERAL OBJECTIVES

This thesis aimed to comprehensively examine the factors that influence sexual function in young women. The main objectives were to understand the interrelationships among these factors and their impact on sexual function. The research also aimed to validate a questionnaire called the Female Sexual Function Index (FSFI) in the Romanian population. Furthermore, the study investigated the effects of autoimmune thyroid diseases (AITD), polycystic ovary syndrome (PCOS), and pregnancy on sexual function. The findings contribute to a better understanding of sexual well-being in young women and can guide the development of interventions and strategies to address sexual difficulties and enhance sexual satisfaction.

2. PRELIMINARY STUDY: PSYCHOMETRIC VALIDATION OF THE ROMANIAN VERSION OF THE FEMALE SEXUAL FUNCTION INDEX (FSFI-RO)

2.1. Aims of the research

This study aimed to analyze the psychometric properties of the Romanian version of the FSFI. The FSFI was selected for its strong psychometric qualities and adaptability to different cultures. The study focused on assessing the reliability and validity of the FSFI in a Romanian-speaking population, aiming to provide a valuable tool for assessing sexual dysfunction in clinical practice and research in Romania.

2.2. Materials and methods

2.2.1. Subjects

The present study included 385 women between the ages of 18 and 51, who were selected from the SCJUPBT Outpatient Endocrinology Clinic in Timisoara, Romania. These women met the criteria of being sexually active for at least 4 weeks prior to the study. Pregnant women and those up to 6 months postpartum, women with neurologic and psychiatric disorders, severe somatic disorders, psychoactive substance abuse or dependence, illiterate women, and women taking medications that could impact sexual functioning were excluded from the study.

2.2.2. Instruments and procedure

This study focused on developing a reliable Romanian version of the FSFI. The translation process involved multiple steps to ensure accuracy, including forward and back translations, expert reviews, and pilot testing for comprehensibility. A total of 50 women participated in the pilot study, reporting no major difficulties in understanding the questionnaire items.

The study employed three instruments: a socio-demographic form, the DSM-5 criteria for sexual dysfunction, and the Romanian Version of the FSFI (FSFI-RO).

Participants completed the FSFI-RO questionnaire, which consisted of 19 items distributed across six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain. The scoring of the questionnaire varied based on Likert scales, and a full-scale score was calculated by summing the scores from all domains. The study also assessed the test-retest

validity of the FSFI-RO by having a subset of participants complete the questionnaire again after a four-week interval.

2.3. Results

The study found that the Romanian version of the FSFI-RO demonstrated good reliability and validity in assessing sexual function in women. The discriminant construct validity analysis showed statistically significant differences between the FSD and control groups, with large effect sizes for arousal, lubrication, orgasm, satisfaction, and the total score. The factor analysis confirmed a six-factor structure, consistent with the original questionnaire, and the internal consistency of the FSFI-RO was strong. Test-retest reliability was high, indicating consistent results over time.

2.4. Discussion

Our study contributes to the field of female sexuality and sexual medicine in Romania, for research, teaching purposes, and clinical practice. By offering a standardized and validated measurement tool for the Romanian population, the FSFI-RO can contribute to more precise diagnosis, treatment planning, and evaluation of treatment outcomes in women facing sexual difficulties. Apart from its diagnostic applications, the Romanian FSFI can be utilized as an outcome measure in clinical trials or intervention studies. Its sensitivity to change enables researchers and clinicians to assess the effectiveness of diverse treatments or interventions for female sexual dysfunction.

2.5. Conclusions

The study findings indicate that the Romanian version of the FSFI-RO demonstrates good psychometric properties similar to the original English version. This confirms that the FSFI-RO is a reliable and valid tool for assessing FSD in Romanian-speaking women. The FSFI-RO effectively measures the same domains of female sexual function as the original questionnaire, making it valuable for both clinical and research purposes in sexual medicine and female sexuality in Romania. Overall, the FSFI-RO has the potential to enhance the quality of life and sexual health outcomes for Romanian-speaking women.

3. STUDY I: THYROID AUTOIMMUNE DISEASE – IMPACT ON SEXUAL FUNCTION IN YOUNG WOMEN

3.1. Aims of the research

The objective of our research was to investigate the sexual function of women with varying degrees of severity of AITD compared to that of healthy women. Additionally, we sought to identify independent predictors for sexual dysfunction among women with AITD.

3.2. Materials and methods

3.2.1. Subjects

The research study involved 320 individuals aged between 20 and 45 years. The study included 250 patients with untreated AITD and 70 healthy females forming the control group. Among the AITD patients, further subdivisions were made based on the level of thyroid dysfunction, resulting in 146 individuals classified as euthyroid (E), 51 individuals classified as having subclinical hypothyroidism (S), and 53 individuals classified as having clinical hypothyroidism (C). The participants were selected from the SCJUPBT Outpatient Endocrinology Clinic in Timisoara, Romania, over a 12-month period.

3.2.2. Clinical and paraclinical evaluation

Patients underwent a comprehensive thyroid assessment, which included clinical examination, neck ultrasound, and laboratory analysis. The laboratory analysis involved measuring TSH, FT4, anti-TPO antibodies, and anti-Tg antibodies. Ovarian assessment was conducted by evaluating medical history, menstrual characteristics, clinical examination, and laboratory assays of estradiol and prolactin.

3.2.3. Psychometric evaluation

At the time of AITD diagnosis, patients completed psychometric scales including the 6-item Female Sexual Function Index (FSFI-6) and the Beck Depression Inventory (BDI-II).

3.3. Results

Patients with AITD had lower scores on the FSFI compared to the control group, and the severity of thyroid disease was associated with an increased risk of sexual dysfunction.

The logistic regression analysis identified higher levels of thyroid-stimulating hormone (TSH) and BDI-II scores as independent risk factors for female sexual dysfunction. A multivariate linear regression analysis showed that TSH and BDI-II scores were significant predictors of sexual dysfunction. A TSH threshold value of 2.75 mIU/L was found to predict FSD with moderate accuracy. The results indicate that higher TSH levels and depression are associated with an increased risk of female sexual dysfunction. The study also established a threshold point for TSH values to predict the diagnosis of sexual dysfunction.

3.4. Discussion

These findings support the role of TSH in the development of FSD and emphasize the importance of considering sexual dysfunction in the diagnostic process of AITD and the need for healthcare professionals to address the sexual problems of female patients with specific clinical conditions. Further prospective control studies are needed for a better understanding of these results.

3.5. Conclusions

Women with AITD have a higher incidence of sexual dysfunction compared to those without the condition, particularly in the areas of sexual desire, lubrication, and orgasm. The severity of hypothyroidism is associated with a decrease in libido and excitability but not with impairments in sexual satisfaction or orgasm. Sexual dysfunction in AITD is closely related to depression, and TSH levels independently contribute to the risk of sexual dysfunction. These findings emphasize the importance of considering sexual health in the diagnosis and treatment of female patients with autoimmune thyroiditis.

4. STUDY II: EFFECTS OF HORMONAL PROFILE, WEIGHT, AND BODY IMAGE ON SEXUAL FUNCTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

4.1. Aims of the research

The objective of our research was to examine the interplay between hormonal, clinical, and psychological factors in the manifestation of sexual dysfunction among women with PCOS.

Previous studies have shown that these patients are at a higher risk of developing sexual problems, such as decreased libido, arousal difficulties, and pain during intercourse. However, the underlying mechanisms of these problems are not well understood.

4.2. Materials and methods

4.2.1. Subjects

The study involved 54 sexually active patients, aged 18 and above, who met at least two of the three Rotterdam criteria for PCOS. These patients, who had not received any prior treatment, were recruited from an outpatient endocrinology clinic in Timisoara, Romania. The study excluded other conditions that could have similar clinical or laboratory manifestations to PCOS, such as thyroid dysfunction, adrenal disorders, and certain medications. Additionally, women with specific medical conditions or psychiatric disorders were also excluded from the study.

4.2.2. Clinical and paraclinical evaluation

During the data collection process, various parameters were obtained to assess and diagnose PCOS. These included age, body mass index (BMI), duration of oligomenorrhea, abdominal circumference (AC), Ferriman-Gallwey (FG) score (evaluating hirsutism), free testosterone (FT) levels, LH/FSH ratio, serum cortisol levels, and ovarian ultrasound findings.

4.2.3. Psychometric evaluation

During the examination, patients were asked to complete two questionnaires: the FSFI and the Body Exposure during Sexual Activities Questionnaire (BESAQ).

4.3. Results

Overweight individuals reported more body image concerns and lower sexual function scores. Correlation analysis revealed an inverse relationship between body weight, body image, and sexual function, particularly in the domains of orgasm, arousal, and desire. Higher BMI, abdominal circumference, and body image concerns were associated with lower sexual function scores. The strongest correlation was found between body image and arousal domain.

Multivariate logistic regression identified the BESAQ score as an independent risk factor for FSD, with elevated scores associated with a 4.24 times higher risk of FSD. Multivariate linear regression further identified FT, BESAQ score, BMI, and LH/FSH ratio as independent predictors of sexual function. Higher FT, BMI, and BESAQ scores were associated with lower sexual function scores, while a higher LH/FSH ratio was associated with higher sexual function scores.

The threshold value for the BESAQ score in diagnosing FSD was determined as 1.97 using ROC curve analysis. Scores above the threshold indicated a positive diagnosis for FSD.

4.4. Discussion

The findings indicated that despite similar hormonal profiles, overweight patients had reduced sexual function and altered body image perception compared to those with normal weight. Hyperandrogenism, indicated by higher levels of free testosterone (FT) and an elevated LH/FSH ratio, was associated with negative effects on sexual function. The study also highlighted the influence of self-esteem, body image perception, and cognitive factors on sexual function, with higher scores on the BESAQ indicating impaired sexual function.

The results suggested a U-shaped effect of testosterone on sexual function, with both hyperandrogenism and testosterone deficiency negatively impacting sexual desire.

4.5. Conclusions

The study findings indicate that excess weight plays a significant role in sexual dysfunction in women with PCOS, beyond the impact of hormonal changes. Body image perception, anxiety, and avoidance behavior related to sexual activities were identified as underlying causes of sexual dysfunction in PCOS patients. The study also revealed a U-shaped effect of free testosterone (FT) on female sexual function, with impairment observed in both FT deficit and excess. This finding has implications for the diagnosis and treatment of sexual dysfunction in PCOS. The BESAQ was found to be a useful tool in diagnosing sexual dysfunction in women with PCOS, along with FT value, LH/FSH ratio, and BMI.

5. STUDY III: THE PARADOX OF SEXUAL DYSFUNCTION OBSERVED DURING PREGNANCY

5.1. Aims of the research

The study aimed to investigate the changes and progression of sexual function during pregnancy and identify the factors contributing to sexual dysfunction among pregnant women.

5.2. Materials and methods

5.2.1. Subjects

The study included 144 pregnant women between the ages of 16 and 45 years, recruited from the Obstetrics and Gynecology Clinic of SCMUT in Timisoara, Romania, over a period of 12 months. Inclusion criteria required participants to be at least 16 years old and to be sexually active. Exclusion criteria were applied to ensure the validity and reliability of the study, excluding women with endocrinological, neurological, or psychiatric disorders that could impact sexual function, as well as those with severe somatic disorders or pregnancy-related complications. Individuals with a history of substance abuse or dependence, illiterate women, and those taking medications that could affect sexual functioning were also excluded.

5.2.2. Instruments and procedure

The study involved three evaluations conducted throughout the pregnancy of the enrolled patients. The initial evaluation occurred around weeks 4-6 of pregnancy. The second and final evaluations took place around weeks 12 and 33-36 of gestation, respectively. During each assessment, the patients completed the FSFI and the BESAQ. In the final evaluation, the patients additionally filled out BDI-II and a questionnaire related to psychological aspects of pregnancy and their relationship with their partner.

5.3. Results

The study found that sexual function, as measured by the FSFI, decreased in the domains of lubrication, satisfaction, pain, and overall score from the first evaluation to the third evaluation during pregnancy. The orgasm domain initially increased but then decreased. There were no significant differences in the desire and arousal domains or in the scores of the BESAQ between evaluations. The prevalence of FSD increased from 17.3% at the initial evaluation to 49.1% at the third evaluation. Women with FSD had a higher history of abortions

compared to those without FSD. Weight status and depression levels were also examined, with underweight women all presenting FSD, and higher BMI values being a protective factor against FSD. Univariate linear regression models showed that relationship satisfaction was a predictor for FSD, and multivariate logistic regression analysis revealed that higher BDI scores and a history of abortion increased the risk of FSD, while being unmarried and having a higher BMI were protective factors.

5.4. Discussion

Hormonal changes and psychological factors such as body image concerns, stress, and anxiety may influence orgasmic experiences. Physical discomfort, body changes, and increased sensitivity can contribute to decreased sexual satisfaction and increased sexual pain or discomfort during pregnancy. The study highlights the complex interplay of hormonal,

The history of abortion may influence sexual well-being through emotional, relationship, and physical factors.

Surprisingly, we discovered that higher BMI was associated with a lower likelihood of sexual dysfunction during the third trimester of pregnancy, contrary to existing literature. The emotional aspect of sexuality may play a significant role in the sexual well-being of overweight or obese pregnant women, potentially explaining this protective effect of higher BMI. However, further research is needed to understand this relationship better and account for sample characteristics.

5.5. Conclusions

Despite the anticipated effects of physical and hormonal changes, subjective factors such as relationship satisfaction, psychological well-being, and emotional aspects of sexuality play a more significant role in influencing sexual function during pregnancy. Low relationship satisfaction, clinical symptoms of depression, and a history of abortion were identified as independent risk factors for sexual dysfunction during pregnancy. Surprisingly, higher BMI was found to have a protective effect against sexual dysfunction in the third trimester of pregnancy, contradicting the general association between BMI and sexual function. These findings emphasize the complexity of sexual function during pregnancy and the importance of considering various factors in its assessment and management.

FINAL CONCLUSIONS

This thesis comprehensively examines various dimensions of sexual function in young women and makes significant contributions to the understanding of physiological, psychological, and body composition factors that influence sexual function. The psychometric validation of the FSFI-RO confirms its reliability and validity for assessing FSD in Romanian-speaking women. The studies within the thesis explore the impact of AITD and PCOS on sexual function, highlighting the role of hormonal, psychological, and body composition factors. The complexities of sexual function during pregnancy are also investigated, emphasizing the influence of subjective factors such as relationship satisfaction, depression, and a history of abortion. The thesis underscores the multi-dimensional nature of sexual function in young women and the need to consider a broader context beyond hormones. It provides evidence-based interventions and strategies to promote healthy sexual development, address sexual difficulties, and enhance sexual satisfaction. The findings have implications for clinical practice and call for further research on additional endocrinological pathologies, menopause, and the long-term impact of sexual dysfunction during pregnancy. Overall, this thesis contributes to a holistic understanding of sexual function in young women and advocates for personalized approaches to improve sexual well-being across different stages of life and diverse populations.

LIST OF PUBLICATIONS

1. **Bortun, A.-M.C.**; Ivan, V.; Navolan, D.-B.; Dehelean, L.; Borlea, A.; Stoian, D. *Thyroid Autoimmune Disease—Impact on Sexual Function in Young Women*. J. Clin. Med. 2021, 10, 369. <https://doi.org/10.3390/jcm10020369>. **(IF=3.303; Indexed in PubMed; PMID: 33478026)**
2. **Daescu, A.-M.C.**; Dehelean, L.; Navolan, D.-B.; Gaitoane, A.-I.; Daescu, A.; Stoian, D. *Effects of Hormonal Profile, Weight, and Body Image on Sexual Function in Women with Polycystic Ovary Syndrome*. Healthcare 2023, 11, 1488. <https://doi.org/10.3390/healthcare11101488>. **(IF=3.16; Indexed in PubMed; PMID: 37239774)**
3. **Daescu, A.-M.C.**; Navolan, D.-B.; Dehelean, L.; Frandes, M.; Gaitoane, A.-I.; Daescu, A.; Daniluc, R.-I.; Stoian, D. *The Paradox of Sexual Dysfunction Observed during Pregnancy*. Healthcare 2023, 11, 1914. <https://doi.org/10.3390/healthcare11131914>. **(IF=2.8; Indexed in PubMed; PMID: 37444748)**