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Original Article / Оригинални рад

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SUMMARY

Introduction/Objective Very little is known about the factors influencing women's attitude towards colposcopy follow-up after cervical treatment. The aim of the study was to investigate the long-term attitude to follow-up colposcopy in women of reproductive age after cervical excision and to evaluate if their attitude was related to their anxiety and depression levels.

Methods Women treated with cervical excision were interviewed after a follow-up colposcopy visit. Their socio-demographic and clinical characteristics were recorded. All women filled in the Beck's anxiety and depression inventory.

Results A total of 160 women were divided into the study group of 42 (26.3%) women who felt discomfort during follow-up colposcopy and the control group of 118 (73.7%) women who did not report such feelings. The mean age of the total sample was 35.3±5.4 years with median time after treatment being 5 years (range:2-18). Women in the study group had significantly lower BMI values, higher rates of nulliparity and nulligravidity, were more often single or living alone and had significantly changed their attitude towards condom use after treatment. Beck's anxiety and depression scores were significantly higher in the study group. Multivariate analysis showed that independent predictors of discomfort during follow-up colposcopy were anxiety levels (OR:1.06; 95%CI:1.00-1.12), living alone or without a partner (OR:2.65; 95%CI:1.08-6.55), and the change in their practice of condom use after treatment (OR:2.69; 95%CI:1.02-7.07).

Conclusion Almost one third of women after excisional treatment reported discomfort during their follow-up colposcopy. These women exhibited higher levels of anxiety.

Keywords: cervical dysplasia; conization; follow-up; colposcopy; anxiety; depression

САЖЕТАК

Увод/Циљ Веома мало се зна о односу жена према колпоскопском праћењу након третмана грлића материце. Циљ студије био је истраживање дугорочног става према колпоскопском праћењу код жена у репродуктивном периоду након ексцизије грлића материце и процена повезаности њиховог става са нивоима анксиозности и депресивности.

Методе Жене лечене ексцизијом грлића материце су интервијуисане након контролног колпоскопског прегледа. Забележене су њихове социо-демографске и клиничке карактеристике. Све жене су попуниле Бекове упитнике за анскиозност и депресију.

Резултати Укупно 160 жена подељено је у студијску групу од 42 (26,3%) жене које су имале непријатност приликом контролног колпоскопског прегледа и контролну групу од 118 (73,7%) које нису осећале непријатност. Просечна старост у укуном узорку била је 35,3±5,4 године, а медијана времена након третмана је била 5 година (распон: 2–18). Жене у студијској групи су имале значајно ниже вредности БМИ, чешће су биле нулипаре и нулигравиде, које су неудате или живе саме и значајно чешће су промениле свој однос према употреби кондома након третмана. Бекови скорови анксиозности и депресивности су били значајно већи у студијској групи. Мултиваријантна анализа је показала да су независни пректори непријатности током контролног колпоскопског прегледа ниво анксиозности (OR:1.06; 95%CI:1.00-1.12), живот ван заједнице или без партнера (OR:2.65; 95%CI:1.08-6.55) и промена праксе употребе кондома након третмана (OR:2.69; 95%CI:1.02-7.07).

Закључак Скоро једна трећина жена након ексизионог третмана навела је непријатност приликом контролног колпоскопског прегледа. Ове жене су имале већи ниво анксиозности.

Кључне речи: цервикална дисплазија; конизација; праћење; колпоскопија; анксиозност; депресивност

INTRODUCTION

The human papillomavirus (HPV) infection affects up to 80% of females during their lifetime [1, 2]. Although most infections are transient, 10 to 20% of women develop a

persistent HPV infection which could cause squamous intraepithelial lesions (SIL) [1]. Low-grade squamous intraepithelial lesions (LSIL) have a high potential for spontaneous regression, while high-grade squamous intraepithelial lesions (HSIL) are to be considered precursor lesions for cervical carcinoma (CC) [3].

SIL is diagnosed mostly during the reproductive age, when most of women have not completed yet their family [4, 5, 6]. Women with HSIL are treated with cervical excision to prevent disease progression into CC, while those with LSIL are treated only in cases of persistent lesions. Following treatment, women are at an increased risk for recurrent SIL and/or CC as compared with the general population thus requiring long-term surveillance [7, 8]. Very little is known about the factors influencing the long-term attitude towards post-treatment follow-up in women who have had excisional cervical treatment for SIL [9, 10].

The objective of our study was to investigate the long-term attitude towards colposcopy follow-up in women of reproductive age at two and more years after excisional cervical treatment of SIL through the process of an interview after a routine follow-up visit at the colposcopy clinic and to evaluate if their attitude was related to their anxiety and depression levels.

METHODS

This was a cross-sectional study that took place in the Colposcopy Unit of the Clinic for Gynecology and Obstetrics Clinical Center of Serbia between April 2014 and October 2016. Our colposcopy service provides long-term follow-up to patients treated for SIL in our institution. The cohort of women in the presented study is the same cohort that was used for the cross-cultural adaptation and psychometric validation of the FACIT-CD questionnaire in Serbian women that was published earlier [11].

We included women who were between 18 to 45 years of age and who received cervical treatment in the form of either cold-knife-conization (CKC) or large loop excision of the transformation zone (LLETZ). The cervical treatment was performed at more than two years prior to this study and squamous intraepithelial neoplasia lesions was histologically confirmed in all participants. We excluded women with a postmenopausal status, who were pregnancy, with a history of previous cervical treatment, who had prior operation on the

reproductive organs except for caesarean section delivery, and with acute gynaecological or other major diseases that could possibly affect their psychological well-being. Women with glandular cervical abnormalities and invasive cervical disease were also excluded.

Participants were interviewed by the first author after their routine follow-up colposcopy examination. The following socio-demographic and clinical data were collected: age, time period from treatment, level of education, employment, marital status, condom use after the treatment, age at menarche, reproductive history and age at the time of treatment. In addition, the body mass index (BMI) of all participants was calculated. The following clinical data were also obtained: indication for the excision (colposcopy/cytology/punch biopsy histopathology), type of treatment (LLETZ/CKC), final histopathology result, postoperative complications, cytology follow-up results and postoperative infertility.

All participants filled in the Serbian version of Beck's anxiety (BAI) and depression (BDI) inventory. Both inventories consisted of 21 questions with a score assigned to each item (range: 0-3). Minimal levels of anxiety correspond with a BAI score of ≤ 7, while minimal levels of depression correspond with a BDI score of ≤ 9, with increasing scores indicating higher levels of anxiety or depression [12].

All women prior to their interview gave written informed consent for the study. The study was approved by the Ethics Committee of the Clinical Centre of Serbia on March 20, 2014 (decision No 541/4).

Statistical data analysis was performed using IBM SPSS Statistics 22 (IBM Corporation, Armonk, NY, USA). Results were presented as frequency (percent), median (range) and mean±SD. For parametric data independent samples t-test was used to test differences between groups. For numeric data with non-normal distribution and ordinal data Mann-Whitney U test was used. Chi-square test or Fisher's exact test was used to test differences between nominal data (frequencies). Predictors of a woman’s attitude towards colposcopy follow-up were analyzed by univariate and multivariate logistic regression. All p values less than 0.05 were considered significant.

RESULTS

A total of 160 patients were divided into two groups: the study group of 42 (26.3%) women feeling discomfort during the follow-up colposcopy examination and the control group of 118 (73.7%) women who did not.

The mean age of the participants was 35.3±5.4 years (range:22-44), with a median equal to 36 at interview. The mean time after the excision was 4.9±3.0 years (range:2-18) with a median of 5 years. Women in the study group had a significantly lower BMI, were more frequently nulliparous and nulligravidae, single or living alone and had changed their attitude towards condom use after the treatment. Four (1.9%) women had BMI ≥30. There were no significant differences detected between the two groups when comparing other characteristics. Table 1 shows the clinical and socio-demographic data of the women at the time point of their interview.

The perioperative and postoperative characteristics of the patients are presented in Table 2. In terms of the type of treatment there was a significant difference among the groups, as women in the study group mainly had LLETZ. CKC was significantly more frequently performed in parous woman, as only six (12.8%) woman who underwent CKC were nulliparous in comparison to 53 (46.9%) in the LLETZ group ($p<0.001$; data not shown). In terms of other characteristics there were no statistically significant differences between the groups.

The majority of the participants had BAI scores ≤7 (n=99 women; 61.9%) and the majority of the participants had BDI scores ≤9 (n=137 women; 85.6%). The average BAI score was 6.92±6.20 in the total sample, 8.81±7.16 in the study group and 6.25±5.70 in the control group, respectively (Figure 1). The average BDI score was 4.37±4.89 in the total sample, 5.74±4.92 in the study group and 3.88±4.81 in the control group, respectively (Figure 2). Significant differences in Beck's anxiety (BAI) and depression (BDI) inventory median scores were detected when comparing the study and the control group: the median BAI score was 6.5 (IQR 9.3, range:0-25) in the study group and 5 (IQR 7, range:0-25) in the control group ($p=0.041$). The median BDI score was 4 (IQR 7.3, range:0-17) in the study group and 2 (IQR 6, range:0-25) in the control group ($p=0.012$). We further compared BAI and BDI scores regarding SIL grade, to evaluate if the anxiety and depression levels that were possibly associated with the SIL grade biased our results. There were no differences between the

patients with LSIL and patients with HSIL groups in relation to median BAI and BDI scores (Table 3).

We further compared BAI and BDI scores regarding SIL grade, to evaluate if the anxiety and depression possibly associated with the SIL grade biased our results.

Multivariate logistic regression analysis showed that discomfort during follow-up colposcopy was independently associated with the change in condom use after the treatment (odds ratio [OR] 2.69, 95% confidence interval [CI] 1.02-7.07), the actual marital status (odds ratio [OR] 2.65, 95% CI [CI] 1.08-6.55), and the BAI score (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.00-1.12) (**Table 4**). Women who had changed their practice of condom use after the treatment, those without a partner and those women with higher anxiety scores had a significantly greater likelihood of feeling discomfort during colposcopy.

DISCUSSION

Women treated for SIL have a long term increased risk for recurrence of the disease, and therefore require long-term surveillance [7,8]. Cytology and/or HPV test, as well as colposcopy are methods of follow-up. Compliance to regular follow-up is essential for timely diagnosis of recurrence. Women's attitude towards follow-up colposcopy may influence attendance of check-ups. In our cohort, 26.3% of women reported that they felt discomfort during follow-up colposcopy after cervical excisional treatment.

Our results demonstrated that women who are nulliparous, nulligravidae, single or living alone represent a population which requires additional interventions to make follow-up procedures for them more acceptable and comfortable. As we did not collect the data on mode of the delivery for women who were parous, we cannot completely rule out if the nulligravidity and nulliparity are the only factors causing discomfort during colposcopy in single women, or it is additionally influenced by the absence of vaginal deliveries in single nulliparous women. Results in relation to type of treatment also raises a question of parity influence on colposcopy discomfort registered in our study, as colposcopy was frequently unpleasant in woman treated with LLETZ, out of which 46.9% were nulliparous. This is consistent with observations that SIL treatment and colposcopy associated distress afterwards in women of childbearing age is more prolonged than initially thought and time-dependent as

a result of their fertility concerns and that it persists until further reproduction is no longer an issue [13]. Moreover, literature data indicate that long-term colposcopy distress is less frequent in women who either had completed childbearing or do not intend to have children [10]. Conversely, Kola and Walsh documented that women having concerns about future fertility reported greater colposcopy-related anxiety levels [14]. Thus, although our findings regarding gravidity and parity were not statistically significant in multivariate analyses, the discomfort perceived by nulligravidae and nulliparous women in our study requires further evaluation.

It would be expected that women with lower BMI values feel less uncomfortable during colposcopy, which was not supported by our results. Patient's BMI in our sample was, on average, within the normal range in both the study and the control group. Therefore, the most probable reason for the difference registered in our study is the small number of obese women in our research (1.9%). In line with this explanation are the results of multivariate analysis, which failed to confirm the influence of BMI on colposcopy discomfort.

It is known that information about the sexually transmitted HPV related disease improves health related behaviors (i.e. use of condoms) [15]. The change in attitude towards condom use between study and control group registered in our cohort can be explained by psychological reasons. We hypothesize that women in the study group may have changed their attitude towards condom use probably due to their fear of HPV re-infection, as it has been described that the use of condoms provides some level of protection against HPV infections [1].

Literature reports indicate that discomfort during colposcopy is psychologically induced, and that this psychological distress is more frequent in women who have already had an abnormal colposcopy result [5, 16]. Psychological distress associated with colposcopy is particularly pronounced in women who have had previous surgical treatment [5].

Women who reported discomfort during colposcopy in our cohort exhibited higher anxiety and depression levels than women not reporting it, regardless of SIL grade. The true time duration of post-treatment adverse psychological outcomes for example anxiety and depression associated with discomfort during post-treatment colposcopy follow-up is yet to be determined. Literature reports available so far have evaluated patients on a relatively short-term basis (up to 30 months) [9]. Moreover, anxiety and depression in patients for

cervical SIL have been documented to decrease with time [14]. It has been documented that lower anxiety levels at the time of colposcopy exam are associated with higher compliance rates, which is paramount in women treated for SIL [17]. These results, in combination with our findings that follow-up colposcopy is more frequently uncomfortable in women with higher anxiety levels indicates that some women may benefit from psychological counseling aiming to reduce anxiety levels and thus prevent possible hindering follow-up adherence. Increased depression levels are also documented to be associated with non-attendance to follow-up, although this was not confirmed by the multivariate analyses in our study, which could be caused by the limited sample size [18].

Reducing anxiety levels during colposcopy decreases the feeling of discomfort during the procedure and improves adherence to follow-up [14, 19]. In line with our results, Baser et al. [19] documented the association between anxiety and discomfort during colposcopy. Additional reasons for unpleasantness documented in the literature are the fear of the associated pain, being naked during the examination and not understanding the physician's explanations, which could also be associated with anxiety [10, 20]. Measures suggested to reduce anxiety and associated feelings of discomfort include listening to music, improving communication with the health practitioner during the examination, obtaining verbal and printed information about the disease and the use of video colposcopy [14, 17, 20, 21]. All the cited authors concluded that reducing anxiety during colposcopy is also beneficial in reducing the rates of loss to follow-up.

Our findings regarding discomfort during follow-up colposcopy and its association with higher levels of anxiety and depression require further longitudinal investigation, as they could be associated with long-term default from post-treatment follow-up which is important as these women have increased risk of developing CC long-term after the treatment [7].

Despite being a single-center cross-section study, meaning that we did not obtain longitudinal data on changes of attitude towards follow-up colposcopy during the years after treatment, we managed to provide an adequate number of years of follow-up after treatment which is the major strength of the study. Moreover, although five different physicians performed the colposcopy exams, all the women were interviewed by a single physician, in the same manner and immediately after colposcopy.

There are certain limitations to this study. First, we recruited woman of reproductive age who underwent follow-up in a single referral hospital. Therefore, our conclusions regarding colposcopy discomfort cannot be applied to all age groups and to untreated women. Secondly, our respondents, undergoing regular check-ups may have had a different health related behavior pattern than those women who do not undergo regular post-treatment check-ups. It is possible that at least some of the women who default from follow-up do it as they experience discomfort and anxiety during follow-up colposcopy.

CONCLUSION

Our results indicate that women of reproductive age reporting colposcopy discomfort after cervical treatment have higher levels of anxiety which are most frequent in these who are single, nulligravidae and nulliparous. There is a need for further research as to the interventions to reduce discomfort, anxiety and depression in women of childbearing age who undergo colposcopy after treatment for cervical dysplasia. Such interventions aiming to reduce discomfort and psychological distress associated with the procedure could possibly lead to increased compliance rates of postoperative surveillance.

NOTE

This paper is part of the doctoral thesis of the first author with title: "Quality of life assessment in women of reproductive age treated for pathological changes in the uterine cervix", which was defended at the School of Medicine, University of Belgrade, on the 13th of June 2018.

Conflict of interest: None declared

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Table 1. Clinical and socio-demographic data of the patients at the time point of their interview.

Data		Total n=160	Study group n=42	Control group n=118	p
CLINICAL DATA					
Age, years (mean ±SD)		35.3±5.4	34.1±5.7	35.8±5.2	0.080
Years after treatment (mean ±SD)		4.9 ± 3.0	4.7±3.2	5.0±3.0	0.492
BMI, kg/m^2 (mean ±SD)		22.2±3.0	21.4±2.2	22.5±3.2	**0.039**
Menarche, years (mean ±SD)		13.2±1.7	13.2±2.0	13.1±1.6	0.796
Abortions, n (%)	0	104 (65.0)	29 (69.0)	75 (63.6)	0.522
	≥1	56 (35.0)	13 (31.0)	43 (36.4)	
Deliveries, n (%)	0	59 (36.9)	22 (52.4)	37 (31.4)	**0.015**
	≥1	101 (63.1)	20 (47.6)	81 (68.8)	
Gravidity, n (%)	0	44 (27.5)	18 (42.9)	26 (22.0)	**0.009**
	≥1	116 (72.5)	24 (57.1)	92 (78.0)	
SOCIO-DEMOGRAPHIC DATA					
Education, n (%)	≤ 12 years	84 (52.5)	23 (54.8)	61 (51.7)	0.732
	> 12 years	76 (47.5)	19 (45.2)	57 (48.3)	
Employment, n (%)	yes	33 (20.6)	8 (19.0)	25 (21.2)	0.769
	no	127 (79.4)	34 (81.0)	93 (78.8)	
Actual marital status, n(%)	single or living alone	54 (33.7)	22 (52.4)	32 (27.1)	**0.003**
	married or coupled	106 (66.3)	20 (46.7)	86 (72.9)	
Condom use after the treatment, n (%)	same	135 (84.4)	31 (73.8)	104 (88.1)	**0.028**
	changed	25 (15.6)	11 (26.2)	14 (11.9)	

BMI – body mass index

Table 2. Perioperative and postoperative characteristics of the patients

Characteristic		Total n=160	Study group n=42	Control group n=118	p
Age at surgery, years (mean ±SD)		30.4±5.0	29.4±5.7	30.8±4.8	0.112
Indication for surgery, n (%)	colposcopy	10 (6.3)	2 (4.8)	8 (6.8)	0.857
	cytology	57 (35.6)	16(38.1)	41 (34.7)	
	histology	93 (58.1)	24 (57.1)	69 (58.5)	
Type of treatment, n (%)	LLETZ	113 (70.6)	35 (83.3)	78 (66.1)	**0.035**
	CKC	47 (29.4)	7 (16.7)	40 (33.9)	
Final histopathology, n (%)	LSIL	43 (26.9)	13 (31.0)	30 (25.4)	0.488
	HSIL	117 (73.1)	29 (69.0)	88 (76.4)	
Postoperative omplications, n (%)	no	134 (83.8)	32 (76.2)	102 (86.4)	0.122
	yes	26 (16.3)	10 (23.8)	16 (13.6)	
Abnormal cytology during follow-up, n (%)	no	126 (78.8)	32 (76.2)	94 (79.7)	0.637
	yes	34 (21.3)	10 (23.8)	24 (20.3)	
Postoperative infertility, n (%)	no	133 (83.1)	37(88.1)	96 (81.4)	0.317
	yes	27 (16.9)	5 (11.9)	22 (18.6)	

LLETZ – large loop excision of the transformation zone; CKC – cold knife conization; LSIL – low-grade squamous intraepithelial lesion; HSIL – high-grade squamous intraepithelial lesion

Table 3. BAI and BDI questionnaire scores in relation to the SIL grade

Score		Total n=160	LSIL n=43	HSIL n=117	p
BAI	≤ 7	99 (61.9%)	24 (58.8%)	75 (64.9%)	0.339
	≥ 8	61 (38.1%)	19 (44.2%)	42 (38.1%)	
BDI	≤ 9	137 (85.6%)	40 (93.0%)	97 (85.6%)	0.105
	≥ 10	23 (14.4%)	3 (7.0%)	20 (14.4%)	

BAI – Beck Anxiety Inventory; BDI – Beck Depression Inventory; LSIL – low-grade squamous intraepithelial lesion; HSIL – high-grade squamous intraepithelial lesion

Table 4. Predictors of the discomfort during colposcopy

Predictor	B	p	OR	95% CI	
				Lower limit	Upper limit
Number of deliveries	0.169	0.552	1.18	0.68	2.07
BMI (kg/m^2)	-0.129	0.089	0.88	0.76	1.02
BAI score	0.058	**0.049**	1.06	1.00	1.12
Barrier contraception use after treatment (changed/same)	0.988	**0.045**	2.69	1.02	7.07
Marital status (single or other/married or coupled)	0.976	**0.034**	2.65	1.08	6.55
Type of treatment (CKC/LLETZ)	-0.864	0.100	0.42	0.15	1.18

BMI-body mass index; LLETZ – large loop excision of the transformation zone; CKC – cold knife conization

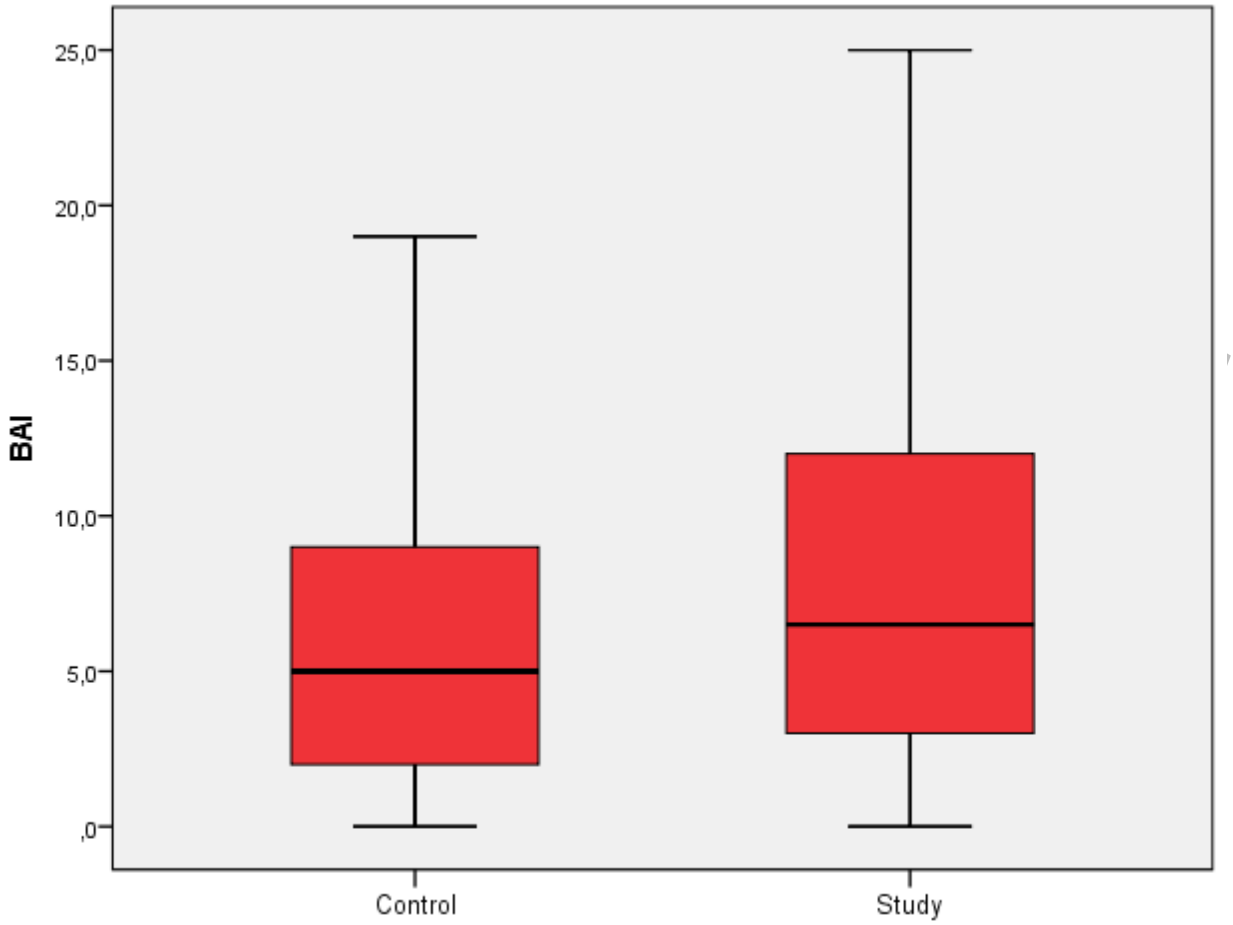

Figure 1. Beck anxiety inventory scores in the study and control group

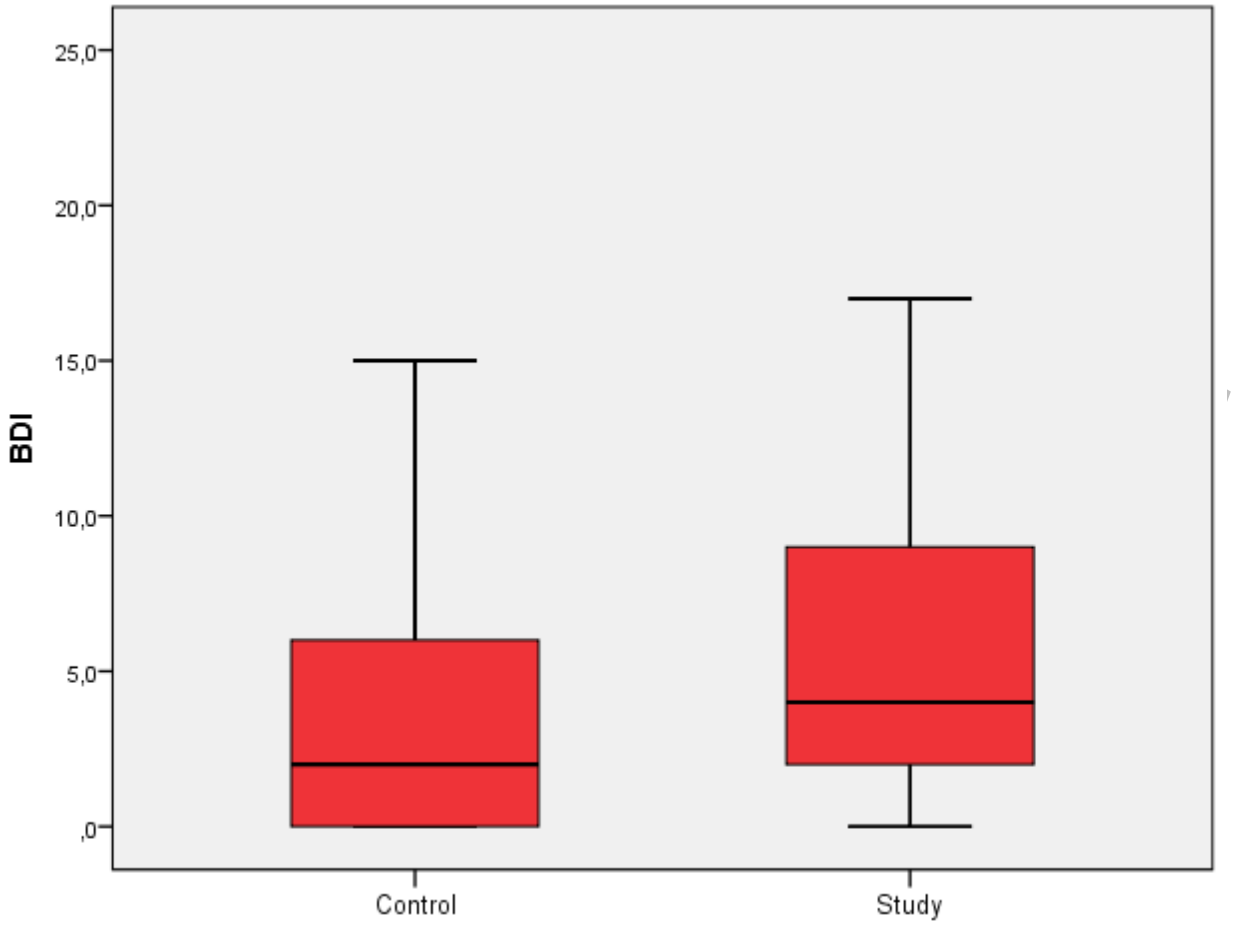

Figure 2. Beck depression inventory scores in the study and control group

