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Psychosocial Impacts of Oral Epithelial Dysplasia

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Abstract

Background: The psychosocial impact of receiving the diagnosis of oral epithelial dysplasia, which presents up to 3.5% increased annual risk of mouth cancer, remain unknown. Using validated instruments, the present study aimed to investigate the prevalence and existing correlations between anxiety, depression and dental anxiety symptoms and burden on oral health-related quality of life.

Methods: A clinical cohort of 82 patients with oral dysplasia was asked to complete the Hospital Anxiety and Depression Scale, the Modified Dental Anxiety Scale and the shortened version of the Oral Health Impact Profile. Spearman's correlation coefficient and regression analyses were performed.

Results: The participants' scores were in keeping with the presence of anxiety, depression and emotional distress symptoms in 30%, 16%, and 26%, respectively. However, 69% experienced anxiety related to procedures that may be required as part of long-term management of oral dysplasia (e.g. local anaesthetic injection). The oral-health related quality of life scores showed 41.5% reporting a recent daily problem due to their oral or dental health. Significant correlations [$p > 0.05$] were found among and between all of the used instruments. Being a female with oral dysplasia also predicted increased odds of indicating higher anxiety and dental anxiety scores than males [$p > 0.05$].

Conclusion: Oral dysplasia can adversely impact on the psychosocial well-being of affected persons. Establishing a causal relationship between the measured variables may, however, be challenging and would need further longitudinal studies.

Introduction

Oral epithelial dysplasia (OED) is defined as a range of cytological and architectural changes in the epithelium, which are associated with an increased risk of progression to squamous cell carcinoma.¹ Management of these potentially malignant epithelial changes is broadly binary, namely conservative management or active treatment. With a lack of consensus on the ideal treatment strategy for OED and the evidence of increased risk of malignant transformation, patients diagnosed with OED have a great deal of uncertainty to contend with following their initial diagnosis. According to Sir William Osler, “Medicine is the science of uncertainty and the art of probability”² and as clinicians we become accustomed to working in an environment of uncertainty³ but we know that this uncertainty can have an impact on the wellbeing of patients.⁴

According to the literature patients with potentially malignant conditions associated with the development of malignant melanoma report that the period of conservative management or ‘watchful waiting’ has a significant impact on the psychological wellbeing and quality of life of patients. With authors strongly recommending the psychological assessment of patients with these potentially malignant conditions.⁵ Patients undergoing investigative procedures of suspected colorectal cancer symptoms experienced anxiety as well as fear and worries regarding a threat to their health.⁶ With less than 20% of patients undergoing an urgent cancer check diagnosed with a malignancy, the level of anxiety and concern is still very high amongst this patient cohort.⁷

Despite the known risk of malignant change in OED and the after mentioned psychosocial impact of potentially malignant conditions on patients, we could find no study in the literature that assess the anxiety, depression and oral health-related quality of life (OHQOL) of patients with OED. The aims of this study were first to use valid and reliable patient-reported tools to assess general anxiety and depression, dental anxiety (DA) and OHQOL among a UK cohort of patients with OED. Secondly, to explore patient demographics and clinical variables that may influence the psychological impact of OED

and finally to evaluate any relationship between anxiety, depression and OHQOL in this patient population.

Patients and methods

Study design and population

This was a cross-sectional and secondary analysis of the data collected from the development and validation of an Oral Epithelial Dysplasia Information Needs Questionnaire (ODIN-Q) study⁸. The study received a favourable opinion from the NHS Health Research Authority [reference: 18/LO/1340]. Eligible participants were adults who aged 18 or above, received the diagnosis of OED based on the histopathological assessment per the 2017 WHO criteria¹ and had no present or recent malignancy in the oral cavity or elsewhere.

Study measures and forms

The 14-item Hospital Anxiety and Depression Scale (HADS)⁹ has presented high internal consistency scores to identify those who their scores of clinical significant for anxiety and depression symptoms in cohorts of patients with oral lichen planus (OLP) [$\alpha = 0.87$ and 0.84]¹⁰ and stomatological diseases [$\alpha = 0.83$ and 0.82].¹¹ HADS includes seven items on each of anxiety (HADS-A) and depression (HADS-D) subscales with a total score for each subscale lies between 0 and 21 that collectively lead to an overall rating between 0 and 42.⁹ The cut-off score of 8 for subscales and 15 for the total scale, respectively.¹⁰

The 5-item Modified Dental Anxiety Scale (MDAS) was preferred over the Corah's scale¹² to assess dental anxiety as the former measures the anaesthesia-related anxiety along with other items. It also showed excellent reliability for the total scale among a cohort of UK general population adults [$\alpha = 0.91$]¹³ and Australian dental clinic attendants [$\alpha = 0.89$].¹⁴ MDAS is scored by 5-point scale (not anxious = 1, extremely anxious = 5). A total cut-off score of 19 or above, out of 25, indicates the need for further management.^{13, 15}

The 14-item Oral Health Impact Profile (OHIP-14)¹⁶ is a well-recognised OHQOL instrument in oral medicine research which presented excellent reliability was shown in

two UK-based clinical studies of OLP [$\alpha = 0.90$]¹⁷ and stomatological disorders including OLP [$\alpha = 0.88$].¹¹ OHIP-14 includes two items in each of the seven domains which are rated by 5-point frequency scale (from never = 0 to very often = 4) and collectively generate a total score ranges between 0 and 56.¹⁶ As no ceiling or cut-off level available for most patient-reported outcome measures, it has been suggested that an individual who indicates one or more selections of OHIP-14 for fairly or very often would indicate a compromised daily activity due to oral or dental health problems.¹⁸

Furthermore, two forms were used to collect additional information about demographics (patient-based) and clinical findings (clinician-based).

Data analyses

The collected data was transferred to the IBM SPSS statistics software (version 22.0) to perform the analytical tests. The frequency and descriptive analyses were calculated for each item, subscale and scale. Based on the Shapiro-Wilk test, the scores were not normally distributed ($p < 0.05$). Therefore, the Spearman's rho (r) coefficient was used to assess the correlations between and within the scales and subscales of each instrument and the respondents' ordinal data.⁹ Results were interpreted as low [≥ 0.20], moderate [≥ 0.40] or high [≥ 0.70].¹⁹

Furthermore, the relationship between the instruments' responses [scores and categories] and patients' demographic and clinical characteristics were assessed using the stepwise linear, binary (forward Wald method) and multinomial logistic regression analyses.²⁰ Cronbach's alpha was calculated for the scales and subscales to assess their inter-item correlation (internal consistency). The results were interpreted as excellent (> 0.90), good (> 0.80), acceptable (> 0.70), questionable (> 0.60), poor (> 0.50) and unacceptable (< 0.50).²¹ All tests were of two-tale and considered of statistical significance if the p-value is less than 0.05.

Results

82, out of the 86 patients who agreed to participate, completed the study questionnaires. The responses from four participants were not included in the analysis due to no response or multiple missing responses. The individual mean imputation method was followed for single missing responses to the HADS (n=1) and OHIP-14 (n=4).²² Participants were 42 females and 40 males with a mean age of 65 (± 11) and mainly of White ethnicity (78%). Most of the participants presented lesions considered as 'low grade' (83%), which mainly affected the tongue (41%) with one or more recorded clinical and/or histopathological diagnoses of oral potentially malignant disorders (OPMDs) (77%) (Table 1).

Assessments of anxiety and depression using HADS in patients with OED

The descriptive analyses for the overall score (HADS-T) showed mean and median scores of 9.6 (± 7.7) and 8.5 out of 42, respectively (Table 2). The categorisation of scores showed that only 16 (19%) and 5 (6%) of participants had definitive scores for anxiety and depression. Scores lying in the doubtful range were less than 20%, whereas those of non-case were of 68% or higher for both subscales. Based on the pre-defined cut-off scores of HADS scale and subscales, HADS-T scores indicated that only 22 out of the 82 participants (26%) presented a score reflecting emotional distress (Figure 1).

Assessments of dental anxiety using MDAS in patients with OED

The descriptive analyses of MDAS scores showed a mean total score of 9.48 (± 4.46) out of the overall score of 20. Concerning MDAS items, 56 (68%) and 57 (69%) of participants had some DA as indicated by MDAS-3 and MDAS-5, respectively (Table 3). Based on the cut-off score of 19, only three participants (3.7%) exceeded this level and therefore considered as dentally anxious. However, there were 9 participants (11%) who had scores that were at the borderline level of 15 or above.

The analyses of OHIP-14 total scores for participants indicated mean and median scores of 11.5 (\pm 10.5) and 8.5, respectively. On a 4-point frequency scale (never to very often), they presented higher mean scores to the two items under the physical domain [*“painful aching in the mouth”* (1.40) and *“uncomfortable to eat any foods”* (1.59)] than others (Table 4). Furthermore, the arbitrary cut-off suggested that 34 of the respondents (41.5%), who chose one or more of ‘fairly often’ or ‘very often’ responses, had problems in the daily life due to their oral health.

Correlations between instruments and the patient’s characteristics

The Spearman’s rho test for ordinal data showed a significant, but weak negative correlation between the older age group and both of HADS-9 [$r = -.244, p = 0.027$] and OHIP-10 [$r = -.219, p = 0$].

Linear regression analyses showed that increased age was negatively related to the total HADS anxiety score; with every year increase of age, there was a 0.57 decrease of the HADS-A scores [$t = -2.20, p = .030$]. In contrast, the number of medications was a positively significant predictor for the HADS-D score; with every additional medication, there was 0.29 increase on HADS-D score [$t = 2.28, p = .025$]. Using the previous test, the number of current oral comorbidities was also a significant but slightly negligible predictor for OHIP-14 total scores; with every additional comorbidity, there was a chance of 0.032 increase on OHIP-14 score [$t = 2.31, p = .024$].

The binary logistic regression showed that being female predicted increased odds of 2.42 to receive higher HADS-A categorical scores (none, mild, moderate or severe) [$B = 1.23, p = .002$] and 0.22 of having higher MDAS scores [$B = 0.199, p = .023$] compared to males. Also, they presented %127 and 84% increased chances of reporting OHQoL issues related to trouble pronouncing any words (OHIP-1) [$B = 0.82, p = 0.033$] and been a bit embarrassed (OHIP-10) [$B = 0.66, p = 0.018$], respectively. Regarding the clinical variables, being symptomatic was a predictor for having higher (worse) scores for HADS-

6 (*feel cheerful*) compared to those who were asymptomatic [OR = 5.76, $p = .021$ (95% CI: 1.29-25.59)].

Compared to other ethnicities (White, Mixed, Black and Chinese), the multinomial logistic regression analyses indicated that Asians were 69% less likely of having increased DA (MDAS) scores [$B = -1.15$, $p = 0.00$ (95% CI: 0.19-0.52)]. Similarly, individuals who currently employed presented 47% less depression (HADS-D) total score [$B = -0.63$, $p = 0.049$ (95% CI: 0.28-0.99)] than those who were unemployed or retired.

Correlations within and between the instruments

The analyses using Spearman's rho coefficients among and between HADS items and those of other instruments showed numerous high ($r \geq 0.70$) and significant ($p > 0.05$) correlations between HADS items. In turn, moderate agreements ($r \geq 0.40$) were found between HADS items and all OHIP items except OHIP-10 (Supplementary File 1). When MDAS items were compared to among each other and with other scales, the only high correlation was found between MDAS-1 and MDAS-2 (Supplementary File 2). Furthermore, the analyses within OHIP items showed a high correlation between OHIP-3 and OHIP-4 as well as between OHIP-9 and OHIP-13 (Supplementary File 1-2).

The reliability coefficients of the assessed scales and subscales were excellent or near excellent Cronbach's alpha values except for functional limitations and psychological disability domains of OHIP-14, which presented a relatively low level of scores (Table 5).

Discussion

In a cohort of 82 patients diagnosed with OED, the present study used validated patient-reported outcome measures to assess of the anxiety and depression, DA levels and OHQOL in terms of presence or absence of attributable symptoms, severity and prevalence rates based on the predefined cut-off scores for each instrument. The prevalence in the present sample was at 30% for anxiety (HADS-A), 16% for depression (HADS-D) and 26% for emotional distress (HADS-T). These rates are generally similar to those of a UK-based study of patients with OLP that reported prevalence rates 39%, 20%

and 27%, respectively.¹⁰ However, they were higher than the rates found among a non-clinical sample in the UK of 12.6% and 3.6% for anxiety and depression using HADS, respectively.²³

The median scores for HADS-A (4.5) and HADS-D (3) were slightly higher when compared to those found in patients with pre-malignant neoplasms of the pancreas (4 and 2, respectively).²⁴ The two highest scored HADS items, '*worrying thoughts go through my mind*' and '*I get a sort of frightened feeling like something awful is about to happen*' were also among the highest scored items in Wiriyakijja's study of OLP.¹⁰ This distress and worry might be predicted with suspected cancerous lesions due to initial symptoms, the uncertainty of the precise diagnosis, the referral process and the implication of the final diagnosis and/or any necessary treatment.^{6, 7}

The present analyses indicated that 3.7% of the respondents had high DA - which is much lower than the range of 8-11% found among population-based studies in the UK and China.^{13, 25} When respondents with borderline scores were included (7.3%), the prevalence rate was presently similar. Moreover, the mean overall score of MDAS (9.49 ± 4.46) was similar to the mean found in new patients attending dental student clinics in Finland (9.44 ± 3.91), Australia (10.76 ± 5.06), UAE (10.90 ± 4.28), but less than similar cohort in Ireland (12.40 ± 5.98).^{14, 15} Also, high scores were previously reported on the tooth being drilled (MDAS-3) and local anaesthetic injection (MDAS-5) with both of the scores to these items being increased among females compared to males.¹⁴ Of note, both items presently received the highest scores, and females were 22% more likely to present higher total MDAS scores.

The assessments of OHQOL using OHIP-14 showed a median global score of 8.5 which was lower than the median noted among 97 patients with stomatological diseases and attending Oral Medicine outpatients' clinics (median = 11) and higher than the UK non-clinical population (median = 2).¹¹ The previous study also indicated worse levels of physical pain and psychological disability domains of OHIP-14 than in a general population which is in line with the present findings. When compared to previous studies of OPMDs and oral cancer, the current mean OHIP-14 score (11.5 ± 10.5) was notably

higher than those found in a cohort of patients in Germany with oral leukoplakia (6.95 ± 10.2), oral squamous cell carcinoma (8.81 ± 8.6) or OLP (9.42 ± 11.4).²⁶

Anxiety, fear and avoidance behaviour to seek dental care can lead to poor oral health and oral health-related quality of life, which could subsequently proceed to a feeling of inferiority and social isolation.^{14, 27} Of note, significant correlations were found between the respondents' scores for HADS, MDAS and OHIP-14, which support the possibility of co-existence of these attributes. In line with the present findings, Yang and colleagues compared HADS and OHIP-14 scores between patients with oral mucosal diseases and healthy control group in China and indicated significant correlations between OHQOL (OHIP-14) and both of anxiety (HADS-A) and depression symptoms (HADS-D) among those with OLP, recurrent aphthous ulcer and the control group.²⁸ Also, correlations of the OHIP-14 domains and HADS-D were found to be significant in individuals with stomatological diseases, whereas those with HADS-A were low or of non-significance.¹¹

The increased prevalence of significant anxiety and depression symptoms in patients with chronic oral mucosal diseases (including the OLP)²⁸ encourage clinicians to use HADS in the day-to-day clinical care of patients with OED to identify and predict those at higher probable risk of anxiety and/or depression and refer these to specialists for therapeutic intervention – when needed. Similarly, MDAS can be a helpful tool for clinicians and health care planners to present appropriate interventions based on the severity of DA and treatment need. OHIP-14 can also help to identify those who have a higher impairment, caused by OED lesions or its associated OPMDs, on aspects of OHQOL such as physical and psychological disabilities, which found to be related to social isolation in patients with oral lesions.²⁹ Nevertheless, these instruments need to be carefully selected, tested and interpreted due to the inherited limitations related to its design and presentation, psychometric properties, clinical interpretability and generalisability of results.³⁰

The study strengths include assessing the anxiety and depression, DA and OHQOL in patients with OED for the first time. The present study also indicated which demographic and clinical characteristics were likely to influence these constructs, which can help clinicians to predict and early recognise patients who are likely to present these

symptoms. Also, the significant correlations between the instruments showed further support to the previous research findings of studies on conditions other than the OED that suggested the associations between the studied constructs.^{11, 27, 28}

Future studies may consider overcoming the limitations of the present study including the relatively low sample size and a lack of control sample for comparisons and non-confirmed clinical diagnoses of anxiety, depression or DA. Also, there was a possible tendency to assess the attributes during a specified reference period (e.g. in the past week or year) of the measured constructs. The longitudinal assessments may, in turn, help to determine whether the diagnosis of OED or different periods of its clinical care, has contributed or increased the levels of these constructs. Although the present analyses showed high internal consistency reliability for pre-validated instruments, the assessments of other essential aspects of reliability (test-retest), validity (structural and criterion), responsiveness and interpretability were not performed.

Although the cause of any relationship between OED and anxiety, depression, dental anxiety and OHQOL, is not known, it is evident that this oral mucosal disease can adversely impact upon the psychosocial well-being of affected persons. Establishing a causal relationship may, however, be challenging and would need further longitudinal studies.

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Conflict of interest

None to declare.

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Table 1. The demographic and clinical characteristics of participants (n=82).

Variable		Category	Number (%)
Demographic characteristics	Ethnicity	White	64 (78%)
		Asians	15 (18%)
		Black	3 (4%)
	Education	Some college and university degree	51 (62%)
		High school diploma or less	26 (32%)
		Not reported	5 (6%)
	Smoking/ alcohol status	Past	45 (55%)/5 (6%)
		Never	28 (34%)/23 (28%)
		Current	9 (11%)/54 (66%)
Degree of	Low grade	68 (83%)	

	dysplasia	High grade	14 (17%)
Clinical characteristics	Site	Tongue	34 (41%)
		Buccal mucosa	22 (27%)
		Upper/lower gingiva	9 (11%)
		Hard and soft palate	7 (8%)
		Lips and labial mucosa	5 (6%)
		Floor of the mouth	5 (6%)
		Associated oral potentially malignant disorder	
Oral leukoplakia	18 (22%)		
Chronic hyperplastic candidosis	4 (5%)		
Oral submucous fibrosis	2 (2%)		
Oral erythroplakia	1 (1%)		
Not recorded	27 (33%)		
History of cancer		No	75 (91%)
		Yes/of which in the oral cavity	7 (9%)/

Table 2. The descriptive analyses of the Hospital Anxiety and Depression Scale.

Item	Mean (SD)/ median	Score distribution							
		0		1		2		3	
		No	%	No	%	No	%	No	%
HADS-A score	5.63 (\pm 4.65)/ 4.5								
<i>HADS1 - feeling tense</i>	0.92 (\pm 0.79)/ 1	25	30	42	51	11	13	4	5
<i>HADS3 - Frightening feeling</i>	0.86 (\pm 1.05)/ 0	42	51	18	22	13	16	9	11
<i>HADS5 - worrying thoughts</i>	1.02 (\pm 0.99)/ 1	30	37	29	35	14	17	9	11
<i>HADS7 - sit at ease</i>	0.75 (\pm 0.76)/ 1	35	43	33	40	13	16	1	1
<i>HADS9 - butterflies in the stomach</i>	0.62 (\pm 0.76)/ 0	42	51	32	39	5	6	3	4
<i>HADS11 - feeling restless</i>	0.79 (\pm 0.76)/ 1	33	40	34	41	14	17	1	1
<i>HADS13 - sudden panic</i>	0.64 (\pm 0.74)/ 0.5	41	50	30	37	10	12	1	1
HADS-D total	3.97 (\pm 3.80)/ 3								
<i>HADS2 - enjoy things</i>	0.70 (\pm 0.82)/ 1	40	49	29	35	10	12	3	4
<i>HADS4 - laugh/see funny side</i>	0.47 (\pm 0.72)/ 0	53	65	20	24	8	9	1	1
<i>HADS6 - cheerful</i>	0.46 (\pm 0.67)/ 0	51	62	25	30	5	6	1	1
<i>HADS8 - slowed down</i>	1 (\pm 0.91)/ 1	27	33	35	43	13	16	7	8
<i>HADS10 - lost interest</i>	0.42 (\pm 0.77)/ 0	59	72	13	16	8	10	2	2
<i>HADS12 -excitement</i>	0.59 (\pm 0.85)/ 0	49	60	21	26	8	10	4	5
<i>HADS14 - enjoy leisure</i>	0.30 (\pm 0.53)/ 0	60	73	19	23	3	4	0	0
TOTAL HADS score	9.60 (\pm 7.76)/ 8.5								

Table 3. The descriptive analyses of the Modified Dental Anxiety Scale.

Item	Mean (SD)/ Median	Score distribution									
		Not Anxious		Slightly Anxious		Fairly Anxious		Very Anxious		Extremely Anxious	
		No	%	No	%	No	%	No	%	No	%
1. Went to the dentist for treatment tomorrow	1.69 (±1)/ 1	47	57	21	26	8	10	4	5	2	2
2. Sitting in the waiting room	1.69 (±1)/ 1	47	57	21	26	8	10	4	5	2	2
3. About to have a tooth drilled	2.26 (±1.2)/ 2	26	32	28	34	13	16	10	12	5	6
4. About to have the teeth scaled and polished	1.59 (±0.95)/ 1	51	62	20	24	6	7	3	4	2	2
5. About to have a local anaesthetic injection in the	2.23 (±1.15)/ 2	25	30	30	37	15	18	7	8	5	6

gum, above an upper back tooth												
Total MDAS score	9.48 (±4.46)/ 8											

Table 4. The descriptive analyses of OHIP-14 items.

Item	Mean (SD)/ median	Score distribution				
		Never	Hardly ever	Occasi onally	Fairly often	Very often
		No (%)	No (%)	No (%)	No %	No (%)
1. Trouble pronouncing any words	0.47 (\pm 0.94)/ 0	61 (74)	9 (11)	8 (10)	2 (2)	2 (2)
2. Sense of taste has worsened	0.70 (\pm 1.15)/ 0	54 (66)	11 (13)	7 (8)	7 (8)	3 (4)
3. Painful aching in the mouth	1.40 (\pm 1.38)/ 1	32 (39)	14 (17)	14 (17)	15 (18)	7(8)
4. Uncomfortable to eat any foods	1.59 (\pm 1.40)/ 2	29 (35)	8 (10)	20 (24)	17 (21)	8 (10)
5. Been self-conscious	1.08 (\pm 1.24)/ 1	39 (48)	14 (17)	16 (19)	9 (11)	4 (5)
6. Felt tense	1.02 (\pm 1.25)/ 0	43 (52)	10 (12)	17 (21)	8 (10)	4 (5)
7. Diet been unsatisfactory	0.79 (\pm 1.19)/ 0	52 (63)	8 (10)	12 (15)	7 (8)	3 (4)
8. Had to interrupt meals	0.75 (\pm 1.00)/ 0	47 (57)	14 (17)	15 (18)	6 (7)	0 (0)
9. Difficult to relax	0.76 (\pm 1.04)/ 0	47 (57)	15 (18)	13 (16)	6 (7)	1 (1)
10. Been a bit embarrassed	0.78 (\pm 1.08)/ 0	48 (58)	13 (16)	14 (17)	5 (6)	2 (2)
11. Been a bit irritable with other people	0.69 (\pm 1.05)/ 0	53 (65)	8 (10)	15 (18)	5 (6)	1 (1)
12. Had difficulty doing the usual jobs	0.46 (\pm 0.81)/ 0	58 (71)	13 (16)	8 (10)	3 (4)	0 (0)
13. Felt that life in general	0.76 (\pm 1.11)/ 0	50 (61)	11 (13)	13 (16)	6 (7)	2 (2)

was less satisfying						
14. Been totally unable to function	0.25 (± 0.64)/ 0	67 (82)	11 (13)	3 (4)	0 (0)	1 (1)
Total score	11.57 (± 10.51)/ 8.5					

Table 5. Cronbach's α of the instruments' scales and subscales.

Instrument	Cronbach's α value	Interpretation
HADS	.914	Excellent
HADS-A	.896	Excellent/good
HADS-D	.836	Good
MDAS	.892	Excellent/good
OHIP-14	.907	Excellent
Functional limitations	.396	Unacceptable
Physical pain	.840	Good
Psychological discomfort	.771	Acceptable
Physical disability	.699	Questionable/acceptable
Psychological disability	.581	Poor
Social disability	.722	Acceptable
Handicap	.684	Questionable

Fig. 1. The distribution of participants' scores based on the cut-off levels of HADS subscales and scale (n=82).

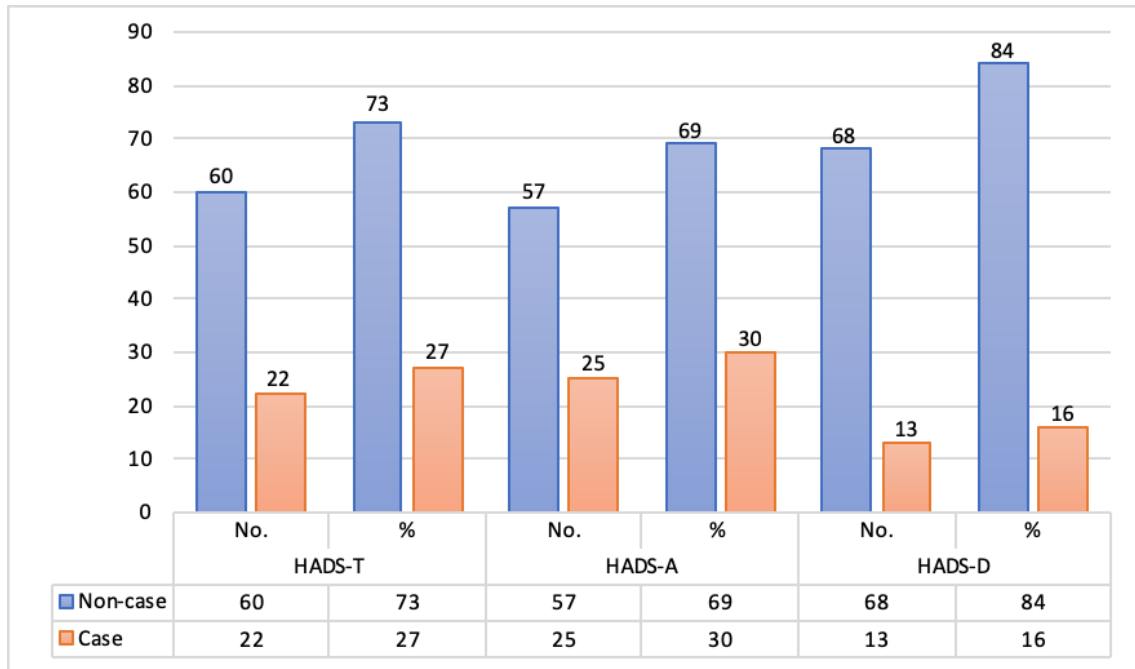


Figure 1. The distribution of participants' scores based on the cut-off levels of HADS subscales and scale (n=82).