

Oral Manifestations of Mucocutaneous Disorders: Exploring Frequency and Oral Health-Related Quality of Life in Egyptian Cohort

Sherin Elsayed*, Wesam Abdel Moneim and Shereen Ali

Department of Oral Medicine and Peridontology, Faculty of Dentistry, Cairo University, Egypt

*Corresponding Author: Sherin Elsayed, Department of Oral Medicine and Peridontology, Faculty of Dentistry, Cairo University, Egypt.

DOI: 10.31080/ASDS.2022.06.1515

Received: October 17, 2022

Published: November 15, 2022

© All rights are reserved by Sherin Elsayed, et al.

Abstract

Background: Literature studying the oral health-related quality of life (OHRQoL) among mucocutaneous disorders are limited. This study counted the frequency of oral manifestations among patients suffering from mucocutaneous disorders and assessed the effect of these oral manifestations on the OHRQoL using Oral Health Impact Profile-14 (OHIP-14).

Methods: The study included adult patients diagnosed with either pemphigus vulgaris (PV), mucous membrane pemphigoid (MMP), erythema multiforme (EM) or Stevens-Johnson syndrome (SJS). We documented patients with oral manifestations during the study and those with previous history. We measured the pain intensity using visual analogue scale (VAS) and OHRQoL by OHIP-14.

Results: Frequencies of oral manifestations were 75%, 62.9%, 76.6% and 26.6%, respectively, among MMP, PV, SJS and EM patients. Patients who reported history of oral manifestations were 18.75%, 9.8%, 6.7% and 22.2%, correspondingly. The frequency of females exceeded the males in all the disorders. MMP patients were the older, while SJS patients were the youngest. EM patients scored the highest VAS score, followed by SJS, then PV and MMP. Concerning OHIP-14 scores, EM scores were the highest followed by SJS, then MMP and PV interchangeably.

Conclusion: The frequency of oral manifestations was high among the studied disorders. Oral manifestations affected the OHRQoL severely, where EM and SJS are associated with the poorest OHRQoL.

Keywords: Mucocutaneous Disorders; Quality of Life; OHRQoL; MMP; PV; SJS; EM; OHIP-14

Introduction

Oral diseases including oral mucosal lesions are considered major public health problems worldwide [17]. As the pattern of oral diseases vary across countries, site specific studies are needed to address the most commonly occurring oral diseases to identify the disease burden and plan for oral health care service [17,18].

This could be more crucial in disorders which require multi-disciplinary patient care such as mucocutaneous disorders [5,9]. Among the most common mucocutaneous disorders; erythema multiforme (EM), mucous membrane pemphigoid (MMP) and pemphigus vulgaris (PV). Though these disorders are commonly observed in practices such as Dermatology and Ophthalmology; oral mucosal lesions may be the initial feature [13,21].

It is fundamental to know patient perception as this could influence selecting appropriate therapeutic regimen and consequently prognosis of the case. Oral health-related quality of life (OHRQoL) is gaining attention among the available patient-centered outcomes [8].

The most validated OHRQoL tool is Oral Health Impact Profile-14 (OHIP-14) [20], additionally it is the second most used patient-reported outcome, after visual analogue scale (VAS), in Oral Medicine literature [15].

We noticed sever scarcity in the studies that assess the frequency of oral mucosal alterations among mucocutaneous disorders in

Egypt. Besides, there is a gap in the literature studying the OHRQoL among patients suffering from these disorders. Accordingly, we decided to perform this study to count the frequency of oral manifestations among patients suffering from mucocutaneous disorders and assess the effect of these oral manifestations on the OHRQoL using OHIP-14.

Materials and Methods

We conducted this cross-sectional study following the principles of the Helsinki Declaration, the study was approved by the Research ethics committee of Faculty of Dentistry, Cairo University (code: 18713). We recruited the participants from the Clinic of Oral Medicine and the Diagnostic Center, Faculty of Dentistry, and Clinic of Dermatology, Faculty of Medicine, Cairo University during the period from August 2018 to February 2019. We applied a convenient consecutive sampling that included all patients fulfilling the eligibility criteria.

Our study included adult patients diagnosed with one of the following mucocutaneous disorder; pemphigus vulgaris, mucous membrane pemphigoid, erythema multiforme and Stevens-Johnson syndrome. Diagnosis was confirmed clinical and histopathological. Other inclusion criteria were accepting to participate in the study and sign the informed consent. Patients complaining from any oral lesions not related to the mucocutaneous disorders and patients who were not physically able to participate were excluded. We enrolled patients in a consecutive order to avoid selection bias. The aim of the study and its importance were clarified to the patients to avoid non-response bias.

For all eligible patients, we carried out thorough conventional oral examination along with charting the demographic data and site of the oral lesions. We recorded if the patient had history of suffering from oral manifestations of the current mucocutaneous disorder.

For patients with detected or suffering from oral manifestation during clinical examination, oral manifestations were identified according to Scully and Felix, 2015 and we documented the site of the lesion [24]. Then, we measured the pain intensity using VAS [10] and OHRQoL by OHIP-14 [25].

VAS ranges from 0 to 10, with 0 indicating “no pain” and 10 indicating “pain as bad as you can imagine” [10]. OHIP-14 is a five-point Likert-type scale. Responses for each question were coded as 0 for “never” response, 1 for “hardly ever” response, 2 for “occasionally” response, 3 for “fairly often” response and 4 for “very often” response [25].

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test when comparing 2 groups and analysis of variance (ANOVA) with multiple comparisons post hoc test when comparing more than 2 groups [3]. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 [3]. Correlations between quantitative variables were done using Pearson correlation coefficient [4]. P-values less than 0.05 were considered as statistically significant.

Results

For the recruitment phase, we assessed 253 patients for eligibility. Three seven patients did not fulfill the eligibility criteria. Two hundred and sixteen patients were eligible to be included.

Our sample included 16 (7.4%) MMP patients, 143 (66.2%) PV patients, 30 (13.9%) SJS patients and 27 (12.5%) EM patients. Table 1 reveals the demographic data.

Frequencies of patients suffering from oral manifestations were 75%, 62.9%, 76.6% and 26.6%, respectively, among MMP, PV, SJS and EM patients. Frequencies of patients who reported history of oral manifestations were 18.75%, 9.8%, 6.7% and 22.2%, correspondingly (Table 2).

Regarding the characteristics of patients suffering from oral manifestations, the frequency of females exceeded the males in all the disorders with no significant difference between the disorders. MMP patients were the older, followed by PV, then EM, while SJS patients were the youngest. A statistical significance difference

	Age			Gender n (%)	
	Mean ± SD	Minimum	Maximum	Male	Female
Mucous membrane pemphigoid	61 ± 6.2	48	71	5 (31.3%)	11 (68.7%)
Pemphigus vulgaris	53.3 ± 6.8	33	69	59 (41.3%)	84 (58.7%)
Steven’s Johnson syndrome	33.6 ± 8.5	16	52	6 (20%)	24 (80%)
Erythema multiforme	31.2 ± 5.7	18	41	8 (29.6%)	19 (70.4%)

Table 1: Demographic data of the studied disorder.
n: Count; %: Frequency; SD: Standard Deviation

Mucocutaneous disorder (n - %)	Presence of oral manifestations	n	%
Mucous membrane pemphigoid (16 - 7.4%)	No oral manifestations	1	6.25
	History of oral manifestations	3	18.75
	Current oral manifestations	12	75
Pemphigus vulgaris (143 - 66.2%)	No oral manifestations	39	27.3
	History of oral manifestations	14	9.8
	Current oral manifestations	90	62.9
Steven’s Johnson syndrome (30 - 13.9%)	No oral manifestations	5	16.7
	History of oral manifestations	2	6.7
	Current oral manifestations	23	76.6
Erythema multiforme (27 - 12.5%)	No oral manifestations	13	48.2
	History of oral manifestations	6	22.2
	Current oral manifestations	8	26.6

Table 2: Frequency of oral manifestations among studied disorders.
n: Count; %: Frequency; SD: Standard Deviation

was obtained between the studied disorders (Table 3). On comparing the disorders to each other’s, we detected a statistically significant difference between each two disorders except EM and SJS (Table S1).

The most affected site in MMP and PV was buccal mucosa, followed by tongue and labial mucosa. For SJS and EM, labial mucosa was the most involved site followed by tongue and buccal mucosa. All MMP, SJS and EM patients suffered from desquamative gingivitis, only half of PV patients suffered from it (Table 3).

n (%)		MMP	PV	SJS	EM	P value
		n (%) mean ± SD [#]	n (%) mean ± SD [#]	n (%) mean ± SD [#]	mean ± SD [#]	
Age [#]		60.42 ± 6.44	52.79 ± 6.36	33.57 ± 9.12	34.75 ± 5.26	< 0.001*
Gender	Male	3 (25.0%)	36 (40.0%)	6 (26.1%)	2 (25.0%)	0.515
	Female	9 (75.0%)	54 (60.0%)	17 (73.9%)	6 (75.0%)	
Pain (VAS) [#]		7.17 ± 0.72	7.44 ± 0.52	7.78 ± 0.42	8.00 ± 0.00	< 0.001*
Site of the lesion	Buccal mucosa	12 (100.0%)	89 (98.9%)	13 (56.5%)	1 (12.5%)	< 0.001*
	Tongue	10 (83.3%)	8 (8.9%)	13 (56.5%)	2 (25.0%)	< 0.001*
	Labial mucosa	5 (41.7%)	32 (35.6%)	23 (100.0%)	8 (100.0%)	< 0.001*
	Desquamative gingivitis	12 (100.0%)	45 (50.0%)	23 (100.0%)	8 (100.0%)	< 0.001*

Table 3: Characteristics of patients suffering from oral manifestations.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome; EM: Erythema Multiforme; VAS: Visual Analogue Scale; n: Count; %: Frequency; SD: Standard Deviation

*: Significant at P ≤ 0.05.

		MMP	PV	SJS	EM
Age	MMP		0.003*	< 0.001*	< 0.001*
	PV	0.003*		< 0.001*	< 0.001*
	SJS	< 0.001*	< 0.001*		1.000
	EM	< 0.001*	< 0.001*	1.000	
Pain (VAS)	MMP		0.479	0.006*	0.003*
	PV	0.479		0.033*	0.023*
	SJS	0.006*	0.033*		1.000
	EM	0.003*	0.023*	1.000	

Table S1: Comparison of age and pain score among the studied disorders.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome; EM: Erythema Multiforme; VAS: Visual Analogue Scale

EM patients scored the highest VAS score, followed by SJS, then PV and MMP. A statistical significance difference was found between the studied disorders (Table 3). On comparing the disorders to each other’s, we identified a statistically significant difference between each two disorders except EM and SJS as well as PV and MMP (Table S1).

Concerning OHIP-14 scores, EM scores were the highest followed by SJS, then MMP and PV interchangeably. We detected a statistical significance difference between the studied disorders for all questions, concepts, and total scores (Table 4,5).

	MMP		PV		SJS		EM		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Q1: trouble pronouncing any words	3.67	0.89	3.58	0.65	4.00	0.74	4.13	0.64	0.020*
Q2: taste has worsened	3.67	0.89	3.58	0.65	4.00	0.74	4.13	0.64	0.020*
Q3: painful aching	3.67	0.89	3.58	0.65	4.00	0.74	4.13	0.64	0.020*
Q4: uncomfortable to eat any foods	3.67	0.89	3.58	0.65	4.00	0.74	4.13	0.64	0.020*
Q5: worried	3.17	1.03	3.54	0.67	4.00	0.74	4.13	0.64	0.002*
Q6: tense	3.17	1.03	3.54	0.67	4.00	0.74	4.13	0.64	0.002*
Q7: diet unsatisfactory	3.58	1.00	3.58	0.70	3.96	0.77	4.25	0.71	0.024*
Q8: interrupt meals	3.58	1.00	3.58	0.70	3.96	0.77	4.25	0.71	0.024*
Q9: difficult to relax	3.58	1.00	3.57	0.65	4.00	0.74	4.13	0.64	0.017*
Q10: embarrassed	2.50	1.09	3.47	0.60	4.00	0.74	4.38	0.74	< 0.001*
Q11: irritable	3.50	1.00	3.57	0.65	4.00	0.74	4.13	0.64	0.014*
Q12: difficulty doing your usual jobs	2.58	0.90	3.40	0.63	3.83	0.72	4.13	0.64	< 0.001*
Q13: life in general was less satisfying	2.58	0.90	3.40	0.63	3.83	0.72	4.13	0.64	< 0.001*
Q14: totally unable to function	1.42	0.51	3.14	0.68	3.78	0.80	4.13	0.64	< 0.001*
Total	44.33	10.59	49.10	8.27	55.35	9.86	58.25	8.66	< 0.001*

Table 4: Scores of OHIP-14 questions.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome; EM: Erythema Multiforme; SD: Standard Deviation

*: Significant at P ≤ 0.05.

	MMP		PV		SJS		EM		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Functional limitation	7.33	1.78	7.16	1.31	8.00	1.48	8.25	1.28	0.020*
Physical pain	7.33	1.78	7.16	1.31	8.00	1.48	8.25	1.28	0.020*
Psychological discomfort	6.33	2.06	7.09	1.35	8.00	1.48	8.25	1.28	0.002*
Physical disability	7.17	1.99	7.16	1.41	7.91	1.53	8.50	1.41	0.024*
Psychological disability	6.08	1.44	7.03	1.15	8.00	1.45	8.50	1.31	< 0.001*
Social disability	6.08	1.78	6.97	1.22	7.83	1.40	8.25	1.28	< 0.001*
Handicap	4.00	1.13	6.54	1.19	7.61	1.47	8.25	1.16	< 0.001*
Total	44.33	10.59	49.10	8.27	55.35	9.86	58.25	8.66	< 0.001*

Table 5: Scores of OHIP-14 concepts.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome;

EM: Erythema Multiforme; SD: Standard Deviation

*: Significant at P ≤ 0.05.

When we compared the disorders to each other’s, we noticed significant difference between the SJS and PV scores of Q1 “trouble pronouncing any words”, Q2 “taste has worsened”, Q3 “painful aching”, Q4 “uncomfortable to eat any foods” and Q9 “difficult to relax” as well as EM and PV scores of Q7 “diet unsatisfactory” and Q8 “interrupt meals”. For Q5 “worried” and Q6 “tense”, we observed significant difference on comparing SJS to MMP as well as PV, and on comparing EM to MMP. Scores of Q10 “embarrassed”, Q12 “difficulty doing your usual jobs”, Q13 “life in general was less satisfying” and Q14 “totally unable to function” showed significant difference on comparing diseases to each other’s except comparing EM to SJS. No significant difference was detected among Q11 “irritable” scores (Table S2).

In addition, individual disorders comparison revealed significant difference between SJS and PV scores of functional limitation and physical pain, EM and PV scores of physical disabilities along with EM and MMP scores of psychological discomfort and social disability. A significant difference was noticed on comparing SJS scores of psychological discomfort, social disability and psychological disability to MMP and PV, additionally on comparing EM scores of psychological disabilities to MMP and PV. Scores of handicaps demonstrated significant difference on comparing diseases to each other’s except comparing EM to SJS (Table S3). As for the total OHIP-14 scores, we detected a significance difference on comparing either SJS or EM to MMP and PV (Table S2).

OHIP-14 questions	Disorders	MMP	PV	SJS	EM
Q1: trouble pronouncing any words	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	
Q2: taste has worsened	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	

Q3: painful aching	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	
Q4: uncomfortable to eat any foods	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	
Q5: worried	MMP		0.541	0.009*	0.025*
	PV	0.541		0.046*	0.184
	SJS	0.009*	0.046*		1.000
	EM	0.025*	0.184	1.000	
Q6: tense	MMP		0.541	0.009*	0.025*
	PV	0.541		0.046*	0.184
	SJS	0.009*	0.046*		1.000
	EM	0.025*	0.184	1.000	
Q7: diet unsatisfactory	MMP		1.000	0.967	0.310
	PV	1.000		0.186	0.048*
	SJS	0.967	0.186		1.000
	EM	0.310	0.048*	1.000	
Q8: interrupt meals	MMP		1.000	0.967	0.310
	PV	1.000		0.186	0.048*
	SJS	0.967	0.186		1.000
	EM	0.310	0.048*	1.000	
Q9: difficult to relax	MMP		1.000	0.593	0.565
	PV	1.000		0.048*	0.200
	SJS	0.593	0.048*		1.000
	EM	0.565	0.200	1.000	
Q10: embarrassed	MMP		< 0.001*	< 0.001*	< 0.001*
	PV	< 0.001*		0.007*	0.003*
	SJS	< 0.001*	0.007*		1.000
	EM	< 0.001*	0.003*	1.000	
Q11: irritable	MMP		1.000	0.290	0.324
	PV	1.000		0.057	0.201
	SJS	0.290	0.057		1.000
	EM	0.324	0.201	1.000	
Q12: difficulty doing your usual jobs	MMP		0.001*	< 0.001*	< 0.001*
	PV	0.001*		0.047*	0.025*
	SJS	< 0.001*	0.047*		1.000
	EM	< 0.001*	0.025*	1.000	

Q13: life in general was less satisfying	MMP		0.001*	< 0.001*	< 0.001*
	PV	0.001*		0.047*	0.025*
	SJS	< 0.001*	0.047*		1.000
	EM	< 0.001*	0.025*	1.000	
Q14: totally unable to function	MMP		< 0.001*	< 0.001*	< 0.001*
	PV	< 0.001*		0.001*	0.001*
	SJS	< 0.001*	0.001*		1.000
	EM	< 0.001*	0.001*	1.000	
Total	MMP		0.481	0.004*	0.004*
	PV	0.481		0.017*	0.033*
	SJS	0.004*	0.017*		1.000
	EM	0.004*	0.033*	1.000	

Table S2: Comparison of OHIP-14 questions score among the studied disorders.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome; EM: Erythema Multiforme

*: Significant at P ≤ 0.05.

OHIP-14 concepts	Disorders	MMP	PV	SJS	EM
Functional limitation	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	
Physical pain	MMP		1.000	1.000	0.890
	PV	1.000		0.049*	0.201
	SJS	1.000	0.049*		1.000
	EM	0.890	0.201	1.000	
Psychological discomfort	MMP		0.541	0.009*	0.025*
	PV	0.541		0.046*	0.184
	SJS	0.009*	0.046*		1.000
	EM	0.025*	0.184	1.000	
Physical disability	MMP		1.000	0.967	0.310
	PV	1.000		0.186	0.048*
	SJS	0.967	0.186		1.000
	EM	0.310	0.048*	1.000	
Psychological disability	MMP		0.083	< 0.001*	< 0.001*
	PV	0.083		0.007*	0.010*
	SJS	< 0.001*	0.007*		1.000
	EM	< 0.001*	0.010*	1.000	
Social disability	MMP		0.183	0.002*	0.003*
	PV	0.183		0.035*	0.055
	SJS	0.002*	0.035*		1.000
	EM	0.003*	0.055	1.000	
Handicap	MMP		< 0.001*	< 0.001*	< 0.001*
	PV	< 0.001*		0.002*	0.002*
	SJS	< 0.001*	0.002*		1.000
	EM	< 0.001*	0.002*	1.000	

Table S3: Comparison of OHIP-14 concepts score among the studied disorders.

MMP: Mucous Membrane Pemphigoid; PV: Pemphigus Vulgaris; SJS: Steven’s Johnson Syndrome; EM: Erythema Multiforme

*: Significant at P ≤ 0.05.

We analyzed the influence of age and gender on pain, OHIP-14 questions, and concepts among all patients suffering from oral manifestations. We noticed a negative correlation between the age and the scores of the studied outcomes (Table S4). Females scored

slightly higher VAS and OHIP-14 scores than males with no significant difference (Table S5). We detected a strong significant positive correlation between the scores of OHIP-14 questions and concepts (Tables S6 and S7).

		Age	
		R	P value
Pain (VAS)		-0.346-	<0.001
Quality of life (OHIP-14 questions)	Q1: trouble pronouncing any words	-0.219-	0.011
	Q2: taste has worsened	-0.219-	0.011
	Q3: painful aching	-0.219-	0.011
	Q4: uncomfortable to eat any foods	-0.219-	0.011
	Q5: worried	-0.350-	<0.001
	Q6: tense	-0.350-	<0.001
	Q7: diet unsatisfactory	-0.210-	0.015
	Q8: interrupt meals	-0.210-	0.015
	Q9: difficult to relax	-0.226-	0.009
	Q10: embarrassed	-0.465-	<0.001
	Q11: irritable	-0.237-	0.006
	Q12: difficulty doing your usual jobs	-0.377-	<0.001
	Q13: life in general was less satisfying	-0.377-	<0.001
	Q14: totally unable to function	-0.438-	<0.001
Quality of life (OHIP-14 concepts)	Functional limitation	-0.219-	0.011
	Physical pain	-0.219-	0.011
	Psychological discomfort	-0.350-	<0.001
	Physical disability	-0.210-	0.015
	Psychological disability	-0.396-	<0.001
	Social disability	-0.325-	<0.001
	Handicap	-0.441-	<0.001
Quality of life	Total	-0.336-	<0.001

Table S4: Influence of age on OHIP-14 questions scores.

Variables	Gender					P value
	Male		Female			
	Mean	SD	Mean	SD		
Pain (VAS)		7.47	0.55	7.53	0.55	0.501
OHIP-14 questions	Q1: trouble pronouncing any words	3.64	0.64	3.72	0.75	0.523
	Q2: taste has worsened	3.64	0.64	3.72	0.75	0.523
	Q3: painful aching	3.64	0.64	3.72	0.75	0.523
	Q4: uncomfortable to eat any foods	3.64	0.64	3.72	0.75	0.523
	Q5: worried	3.55	0.72	3.66	0.78	0.426
	Q6: tense	3.55	0.72	3.66	0.78	0.426
	Q7: diet unsatisfactory	3.62	0.64	3.72	0.82	0.455
	Q8: interrupt meals	3.62	0.64	3.72	0.82	0.455
	Q9: difficult to relax	3.64	0.64	3.70	0.77	0.653
	Q10: embarrassed	3.43	0.71	3.58	0.85	0.286
	Q11: irritable	3.64	0.64	3.69	0.77	0.718
	Q12: difficulty doing your usual jobs	3.38	0.68	3.48	0.79	0.494
	Q13: life in general was less satisfying	3.38	0.68	3.48	0.79	0.494
	Q14: totally unable to function	3.09	0.86	3.20	0.97	0.506
OHIP-14 concepts	Functional limitation	7.28	1.28	7.44	1.49	0.523
	Physical pain	7.28	1.28	7.44	1.49	0.523
	Psychological discomfort	7.11	1.43	7.33	1.55	0.426
	Physical disability	7.23	1.29	7.44	1.64	0.455
	Psychological disability	7.06	1.19	7.28	1.44	0.384
	Social disability	7.02	1.22	7.16	1.49	0.580
	Handicap	6.47	1.41	6.67	1.65	0.470
Total Quality of life score		49.45	8.33	50.77	9.93	0.440

Table S5: Influence of gender on pain, OHIP-14 questions and concepts.

SD: Standard Deviation

*: Significant at P ≤ 0.05.

		Functional limitation	Physical pain	Psychological discomfort	Physical disability	Psychological disability	Social disability
Physical pain	r	1.000	--				
	P value	< 0.001*					
Psychological discomfort	r	0.801	0.801	--			
	P value	< 0.001*	< 0.001*				
Physical disability	r	0.912	0.912	0.740	--		
	P value	< 0.001*	< 0.001*	< 0.001*			
Psychological disability	r	0.860	0.860	0.873	0.830	--	
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*		

Social disability	r	0.927	0.927	0.807	0.870	0.887	--
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	
Handicap	r	0.680	0.680	0.712	0.636	0.779	0.859
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*

Table S6: Correlation between OHIP-14 concepts.

r: Correlation Coefficient

*: Significant at P ≤ 0.05.

		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Q2	R	1.000	--											
	P value	< 0.001*												
Q3	R	1.000	1.000	--										
	P value	< 0.001*	< 0.001*											
Q4	R	1.000	1.000	1.000	--									
	P value	< 0.001*	< 0.001*	< 0.001*										
Q5	R	0.801	0.801	0.801	0.801	--								
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*									
Q6	R	0.801	0.801	0.801	0.801	1.000	--							
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*								
Q7	R	0.912	0.912	0.912	0.912	0.740	0.740	--						
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*							
Q8	R	0.912	0.912	0.912	0.912	0.740	0.740	1.000	--					
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*					
Q9	R	0.986	0.986	0.986	0.986	0.788	0.788	0.926	0.926	--				
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*				
Q10	R	0.566	0.566	0.566	0.566	0.766	0.766	0.570	0.570	0.582	--			
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*			
Q11	R	0.979	0.979	0.979	0.979	0.781	0.781	0.919	0.919	0.993	0.587	--		
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*		
Q12	R	0.783	0.783	0.783	0.783	0.749	0.749	0.734	0.734	0.794	0.651	0.798	--	
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	
Q13	R	0.783	0.783	0.783	0.783	0.749	0.749	0.734	0.734	0.794	0.651	0.798	1.000	--
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Q14	R	0.512	0.512	0.512	0.512	0.594	0.594	0.478	0.478	0.528	0.640	0.551	0.734	0.734
	P value	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*

Table S7: Correlation between OHIP-14 questions.

Discussion

Oral mucosa seems to be one of the most affected mucous membranes in mucocutaneous disorders and commonly represents the site of disease onset. However, the available data about the oral manifestations in these disorders is not sufficient [1,6,13,21].

Only twenty countries investigated the frequency of oral manifestations in PV. Although Egypt was among these countries, it was only single study [1]. The objective of the study was primarily to determine the prevalence of Ear, nose, and throat involvement. They documented that the frequency of the oral symptoms was 67.6% among the studied thirty-four patients [7].

The frequency of oral mucosal lesions in the current study reached to 72.7%. This frequency sits in the prevalence range concluded in a recent systematic review [1]. In addition, our frequency was comparable to that reported by Calabria, *et al.* 2020 [2].

The policy of the WHO Global Oral Health Program emphasizes that oral health is integral and essential to general health, and that oral health is a determinant factor for quality of life (QoL) [19]. We noticed rarity in the literature studying the OHRQoL among patients suffering from the currently studied mucocutaneous disorders, if any in some disorders. Up to our knowledge, the current study is the first to assess OHRQoL via OHIP-14 in this population and the first to investigate OHRQoL in a sample of MMP, EM and SJS patients.

PV was the most investigated [11,12,16,23,26] couple of studies included few MMP patients [11,23]. The conducted studies used dermatology specific or general health tools for the QoL. Moreover, oral mucosal involvement was not given the requested attention [11,12,16,22,23,26].

The results of the current study confirm the importance of considering the effect of oral manifestations on the QoL. The frequency of oral mucosal involvement was high, it exceeded 90% in MMP, either detected during examination or reported by the patient. Thus, oral mucosal manifestations of these disorders require more consideration and engagement of oral medicine specialists is crucial.

In the current study, PV patients suffered from poor OHRQoL. This is in consensus with the studies that documented the impact of PV on the QoL [11,12,16,22,23,26].

Two studies highlighted the effect of the mucosal involvement, they stated that mucosal manifestations had a great impact on the essential activities as speaking or eating [26] and they observed that mucosal pemphigus disease area index score was correlated with the QoL [12]. Accordingly, Krain, *et al.* 2019 advised researchers to assess QoL among PV with mucosal involvement.

A recent study investigated QoL using general questionnaire (SF-36) in oropharyngeal PV patients. They documented poor QoL among the patients particularly limited work and daily activities which affected physical and emotional health [2].

Single study found that PV patients had poorer QoL than MMP [11]. In the current study, PV patients scored higher OHIP-14 score than MMP patients, but the scores of MMP were near those of PV.

Two studies assessed the QoL in patients suffering from chronic oral mucosal disorders in limited samples. [14,20]. The first study investigated a purposive sample composing of 24 patients among them two PV patients and two MMP patients. They used qualitative interviewing method [14]. The second study grouped their patients as oral lichen planus, aphthous stomatitis, PV and the fourth group included other disorders including SJS. However, they did not mention the number of SJS patients. The authors observed that PV had the poorest QoL among the studied groups. The outcome measured in this study was Chronic Oral Mucosal Diseases Questionnaire [20].

From our results, it is notable that EM and SJS caused poorer OHRQoL compared to MMP and PV. In each disorder, the scores of OHIP-14 concepts were comparable. Still, we noticed that physical and psychological disabilities were the most affected in EM, functional limitation along with physical pain and disability were the most affected in PV and MMP, finally handicap was the least affected in all the studied disorders. VAS revealed that EM oral lesions was the most painful followed by SJS, PV and MMP.

Concerning the influence of age and gender on the OHRQoL scores. We noticed a negative correlation with the age and females reported poorer OHRQoL compared to males. Earlier data is heterogenous. Some researchers documented that age and gender had no influence on the QoL scores [23,26]. Other found that females and old patients had poorer QoL [16,20].

From the current results, we can conclude that the frequency of oral manifestations was high among MMP, SJS and PV. Buccal mucosa was the most affected site in MMP and PV, while labial mucosa was the most affected site in SJS and EM. Desquamative gingivitis was common among MMP, SJS and EM patients. Oral manifestations of the studied mucocutaneous disorders affected the OHRQoL severely, where EM and SJS are associated with poorer OHRQoL than MMP and PV. We recommend conducting further studies with larger sample size and a control group.

Conclusion

In the end, we hope that this study can serve as a baseline to highlight the role of Oral Medicine specialists in the diagnosis and management of these disorders, reinforce the importance of multidisciplinary diagnosis and management which can help in the prognosis of these cases.

Recommendation

The high prevalence of oral manifestations among mucocutaneous ocular disorders in Egypt suggests that active participation of oral medicine practitioners in the long term follow up of these patients is likely to significantly affect not only the proper management of oral ulcers, but also the establishment of other diagnoses and treatment strategies.

Further studies on large samples and different designs are recommended to help in diagnosis and management of the oral manifestations of mucocutaneous ocular disorders patients as they are very common and have a dramatic effect on the patient's quality of life.

Author Contributions

Wesam Abdel Moneim and Shereen Ali: concept and design. Sherin Elsayed: acquisition of data. Shereen Ali: analysis and interpretation of data. Sherin Elsayed, Wesam Abdel Moneim, and Shereen Ali: drafting and revising of the manuscript.

Bibliography

1. Batistella Elis Ângela, *et al.* "Prevalence of oral mucosal lesions in patients with pemphigus vulgaris: A systematic review and meta-analysis". *Journal of Oral Pathology and Medicine: Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology* 50.8 (2021): 750-757.
2. Calabria Elena, *et al.* "Autoimmune mucocutaneous blistering diseases in the south of Italy: a 25-year retrospective study on 169 patients". *Journal of Oral Pathology and Medicine: Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology* 49.7 (2020): 672-680.
3. Chan YH. "Biostatistics 102: quantitative data--parametric and non-parametric tests". *Singapore Medical Journal* 44.8 (2003): 391-396.
4. Chan YH. "Biostatistics 104: correlational analysis". *Singapore Medical Journal* 44.12 (2003): 614-619.
5. Esatoglu, Sinem Nihal *et al.* "Behçet's syndrome: providing integrated care". *Journal of Multidisciplinary Healthcare* 10 (2017): 309-319.
6. Farthing P, *et al.* "Mucosal disease series. Number IV. Erythema multiforme". *Oral Diseases* 11.5 (2005): 261-267.
7. Fawzy Marwa Mohamed, *et al.* "Ear, nose, and throat involvement in Egyptian patients with pemphigus vulgaris: a step towards a better management". *International Journal of Dermatology* 52.10 (2013): 1268-1273.
8. Hegarty AM, *et al.* "Patient-centred outcome measures in oral medicine: are they valid and reliable?". *International Journal of Oral and Maxillofacial Surgery* 31.6 (2002): 670-674.
9. Hatemi Gulen, *et al.* "Considerations in designing and interpreting prevalence studies for Behçet syndrome". *Polish Archives of Internal Medicine* 128.3 (2018): 148-149.
10. Huskisson, E C *et al.* "Application of visual-analogue scales to the measurement of functional capacity". *Rheumatology and Rehabilitation* 15,3 (1976): 185-187.
11. Kalinska-Bienias Agnieszka, *et al.* "Measuring of quality of life in autoimmune blistering disorders in Poland. Validation of disease - specific Autoimmune Bullous Disease Quality of Life (ABQOL) and the Treatment Autoimmune Bullous Disease Quality of Life (TABQOL) questionnaires". *Advances in Medical Sciences* 62.1 (2017): 92-96.
12. Krain Rebecca L, *et al.* "Assessing the Correlation Between Disease Severity Indices and Quality of Life Measurement Tools in Pemphigus". *Frontiers in Immunology* 10 (2016): 2571.

13. Leuci Stefania, *et al.* "Oral autoimmune vesicobullous diseases: Classification, clinical presentations, molecular mechanisms, diagnostic algorithms, and management". *Periodontology 2000* 80.1 (2019): 77-88.
14. Ni Riordain R., *et al.* "Impact of chronic oral mucosal disease on daily life: preliminary observations from a qualitative study". *Oral Diseases* 17.3 (2011): 265-269.
15. Ní Ríordáin, Rícheal, *et al.* "World Workshop on Oral Medicine VI: Patient-reported outcome measures and oral mucosal disease: current status and future direction". *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology* 120.2 (2015): 152-160.e11.
16. Paradisi, Andrea *et al.* "Quality-of-life assessment in patients with pemphigus using a minimum set of evaluation tools". *Journal of the American Academy of Dermatology* 60.2 (2009): 261-269.
17. Petersen Poul Erik, *et al.* "The global burden of oral diseases and risks to oral health". *Bulletin of the World Health Organization* 83.9 (2005): 661-669.
18. Petersen Poul Erik. "The World Oral Health Report 2003: continuous improvement of oral health in the 21st century--the approach of the WHO Global Oral Health Programme". *Community Dentistry and Oral Epidemiology* 31.1 (2003): 3-23.
19. Petersen Poul Erik. "Global policy for improvement of oral health in the 21st century--implications to oral health research of World Health Assembly 2007, World Health Organization". *Community Dentistry and Oral Epidemiology* 37.1 (2009): 1-8.
20. Rajan Bijina, *et al.* "Assessment of quality of life in patients with chronic oral mucosal diseases: a questionnaire-based study". *The Permanente Journal* 18.1 (2014): e123-127.
21. Rashid Hanan, *et al.* "Oral Lesions in Autoimmune Bullous Diseases: An Overview of Clinical Characteristics and Diagnostic Algorithm". *American Journal of Clinical Dermatology* 20.6 (2019): 847-861.
22. Riva Federico, *et al.* "Adult oral health-related quality of life instruments: A systematic review". *Community Dentistry and Oral Epidemiology* 50.5 (2022): 333-338.
23. Saleh Marwah Adly, *et al.* "Assessment of the quality of life of Egyptian and Tunisian autoimmune bullous diseases' patients using an Arabic version of the autoimmune bullous disease quality of life and the treatment of autoimmune bullous disease quality of life questionnaires". *Anais Brasileiros de Dermatologia* 94.4 (2019): 399-404.
24. Scully C and D H Felix. "Oral medicine--update for the dental practitioner. Mouth ulcers of more serious connotation". *British Dental Journal* 199.6 (2005): 339-343.
25. Slade GD and A J Spencer. "Development and evaluation of the Oral Health Impact Profile". *Community Dental Health* 11.1 (1994): 3-11.
26. Sung Jae Yong, *et al.* "Quality of Life Assessment in Korean Patients with Pemphigus". *Annals of Dermatology* 27.5 (2015): 492-498.