

Oral Candidiasis and Nutritional Status in Hospitalized Aged Patients: A Cross-sectional Study in Cuenca-Ecuador

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ABSTRACT

Background: Oral candidiasis (OC) is an opportunistic fungal disease related to various local and systemic factors. Hospitalized aged patients are considered susceptible hosts with several adverse clinical outcomes, including OC and undernutrition.

Aims: The aim of this study was to determine the prevalence of oral candidiasis among hospitalized aged patients who attended on the inpatient units of Vicente Corral Moscoso Hospital and Jose Carrasco Arteaga Hospital of Cuenca-Ecuador. And also, to evaluate the association between OC and nutritional status in hospitalized aged patients.

Methods and materials: This study was performed with two hundred and twenty subjects; convenience sampling was applied for seven months. Demographic data were collected by a questionnaire. OC diagnosis was accomplished by oral examination; clinical lesions suggestive were analyzed with swabbed culture tests. OC was diagnosed when patients exhibited oral suggestive lesions synchronously with positive culture results. Nutritional assessment was performed with Controlling Nutritional Status (CONUT) system. Statistical analysis was performed with IBM_SPSS-20 software; associations were analyzed using Chi-square test, or Fisher's exact test, and multiple logistic regression. For all tests, $p \leq 0.05$ was considered as a statistically significant result.

Results: Out of 220 hospitalized aged patients, 62 (28.1%) were diagnosed with oral candidiasis. The mean age was 78.3 ± 7.8 years. The Demographic/clinical variables (sex, age, residence area, education, use of dental prostheses) indicated no correlation with oral candidiasis. Nutritional variables (hypoalbuminemia and severe undernutrition) were significantly correlated with oral candidiasis ($p=0.009$; $p=0.007$).

Conclusions: 28.1 % of the hospitalized aged patients had oral candidiasis. Hypoalbuminemia and severe undernutrition are risk factors associated with oral candidiasis.

Keywords: Aged, Oral candidiasis, Nutritional status, Undernutrition.

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I. INTRODUCTION

Oral candidiasis (OC) is an opportunistic infection of the oral cavity [1], which has been extensively explored in the literature. Many studies have investigated the relationship between this fungal disease and its local and systemic modulation factors, such as poor oral health, wearing dental prostheses, xerostomia, drugs, chronic diseases, endocrine disorders, malignancies, nutritional factors, and immunosuppressive conditions [2]-[6].

OC is a significant infection in immunosuppressed patients [7]. Particularly, the effects of aging on immune function can result from changes in immune cells [8]. Considerable changes in the expression of CD11b in neutrophils and CD40

in B lymphocytes have been demonstrated in the elderly; these alterations can result in an impairment of phagocytic capacity and a decline in B lymphocyte activation [8]. Hence, immunosenescence, is a complex remodeling process that can become a significant predisposing factor to the increased risk and severity of infections in older people [9]. Consequently, the prevalence of infections increases with age [10].

Meanwhile, the world is expected to experience a significant acceleration in the speed of population aging over the coming years [11]. A projection of the United Nations affirms that in the Latin American and Caribbean regions, the number of people aged 60 and older is predicted to increase from 11% to 12% to more than 25% by 2050 [12].

Nevertheless, the increase in life expectancy coexists with chronic, malignant, and degenerative diseases which have also led to an increase in hospitalizations of the elderly population [13]. Thus, hospitalized aged patients should be considered a risk population to develop many clinical adverse events.

In addition, undernutrition is a highly prevalent condition in this group [14], [15]. Nevertheless, up to our knowledge, no significant work has been published for epidemiological data linking OC with undernutrition in hospitalized aged patients. Knowledge on this subject remains unsatisfactory since insufficient studies have addressed this correlation.

To corroborate the aforementioned findings and to elucidate this correlation, the aim of this study was to determine the prevalence of OC and also, to evaluate the association between OC and nutritional status in hospitalized aged patients.

II. METHODS AND MATERIALS

A. Study Design and Population

This analytical cross-sectional study was performed on aged patients who attended the inpatient units of Vicente Corral Moscoso Hospital and Jose Carrasco Arteaga Hospital of Cuenca-Ecuador.

Sample size calculation was done using a total of 900 inpatients registered in the statistics hospital files. Considering a margin of error of 5%, a confidence level of 95%, and an expected risk factor frequency of 25%, we required sample size of two hundred and eighteen participants [16].

Finally, two hundred and twenty (220) subjects were invited to participate in this study. To enroll the participants, convenience sampling (non-probability technique) was used.

B. Including / Excluding Criteria

Male or female subjects 65 years of age or older were included. Participants with hematological neoplasms, undergoing radiotherapy and /or chemotherapy, immunosuppressive treatments, and severe physical or cognitive limitations were excluded.

C. Study Method

Subjects were described by demographic/clinical (e.g., sex, age, residence area, education, dental prostheses, years of use of dental prostheses, and oral candidiasis) and nutritional variables (e.g., serum albumin, total lymphocyte, total cholesterol, and nutritional status performed by the "Controlling Nutritional Status", CONUT system) [17].

The present study was confirmed in accordance with Declaration of Helsinki. Each participant was informed in detail about the objectives of the research.

All the participants expressed their acceptance to participate in this study through the informed consent form designed for this purpose. This study was approved by the School of Medicine, University of Cuenca Ethical Committee (UC-FCMMIS-2016-0215-M).

D. Nutritional Status Assessment

The nutritional status was estimated by applying the CONUT scoring system. It was performed based on the

serum albumin concentration, total peripheral lymphocyte count, and total cholesterol level, which are representative hematological markers of protein reserves, impaired immune defenses and calorie deficiency, respectively [18]-[23].

To obtain the CONUT score, independent blood parameters were summarized in Table I. The total scores ranged from 0 to 12 and classified the subjects into four groups: normal nutritional status (0-1 point), light undernutrition (2-4 points), moderate undernutrition (5-8 points), and severe undernutrition degree (9-12 points). The blood samples were processed in the hospital laboratories and, the results were extracted from the patient's records.

TABLE I: NUTRITIONAL STATUS ACCORDING TO CONUT SYSTEM [17]

Parameter				
Serum albumin (g/dL)	≥3.5	3.0-3.49	2.5-2.9	<2.5
Score	0	2	4	6
Total lymphocytes (/mm ³)	≥1600	1200-1599	800-1199	<800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140-180	100-139	<100
Score	0	1	2	3
CONUT Score	0-1	2-4	5-8	9-12
Interpretation	Normal	Light	Moderate	Severe

E. Intra Oral Examination and Diagnosis of Oral Candidiasis

Subjects were examined by a single dentist (Y.P-B.) using a head-light and a sterilized dental mirror. Dental prostheses and the presence of suggestive lesions of OC were verified. This procedure was performed without knowledge of patients' nutritional status. Previously, the examiner was particularly trained to recognize suggestive lesions of OC (kappa coefficient=0.82).

In this sense, lesions such as whitish creamy plaques, red smooth mucosa, well-delimited adherent homogeneous or nodular white plaques, erythema restricted to the denture supporting area, the erythematous rhomboid-like area located on the midline of the dorsum of the tongue, and erythematous and fissured lesions affecting the corners of the mouth were considered as suggestive lesions of OC [24].

The suspected areas were scraped with a sterile cotton swab (Citoswab, CITOTEST Labware Manufacturing Co., Ltd., ISO13485, Jiangsu, China). The swabs were inoculated onto Sabouraud dextrose agar (HiMedia Laboratories Private Limited, MH063, Mumbai, India). Next, the plates were incubated aerobically at 36±0 °C for a minimum of 72 hours.

The formation of luxuriant, convex, whitish, cottony yeast colonies was considered as positive culture results. OC was diagnosed when patients exhibited oral suggestive lesions synchronously with positive culture results in the microbiological analysis.

F. Statistical Analysis

All statistical analysis was performed using EpiInfo statistical software and Statistical Package for Social Sciences (SPSS, version 22, IBM Corporation, Armonk, NY, EEUU).

Categorical variables were described as numbers and percentages. Statistical associations between OC and demographic/clinical and nutritional variables were analyzed using the chi-squared test (χ^2) or Fisher's exact test, and

multinomial logistic regression. For all tests, $p \leq 0.05$ was considered as a statistically significant result.

III. RESULTS

Table II shows the demographic analysis of 220 hospitalized aged patients. Our findings indicated a slight female predominance of 50.45% (n=111). The patients' ages ranged from 65 to 98 years (mean 78.3 \pm 7.8 years). Most subjects 54.09% (n=119) resided in rural areas and 89.50% (n=197) attended primary education or did not reach any educational level.

TABLE II: HOSPITALIZED AGED PATIENTS BY DEMOGRAPHIC VARIABLES (N=220)

Variables	n	%
<i>Sex</i>		
Female	111	50.45
Male	109	49.55
<i>Age groups</i>		
65–79 years	116	52.73
≥ 80 years	104	47.27
<i>Residence area</i>		
Rural	119	54.09
Urban	101	45.91
<i>Education</i>		
None /primary education	197	89.55
Secondary/ tertiary education	23	10.45

Mean age: 78.3 \pm 7.8 years.

The present study also demonstrates that 60.4% (n=133) of the participants had decreased values of serum albumin, 69.0% (n=152) presented a reduced lymphocyte count, and 55.4% (n=122) had a deficit of total cholesterol levels.

The assessment of nutritional status according to the CONUT system revealed that only 18.2% (n=40) of the hospitalized aged patients had a normal nutritional status (0-1 point). It should be noted that most of the subjects 36.4% (n=80) had a light undernutrition degree with a score between 2-4 points, 35% (n=77) presented moderate undernutrition degree (5-8 points) and 10.5% (n=23) revealed a severe undernutrition degree (9-12 points).

Table III summarizes the nutritional characteristics of the study population.

TABLE III: HOSPITALIZED AGED PATIENTS BY NUTRITIONAL VARIABLES (N=220)

Variables	n	%
<i>^a Serum albumin</i>		
Normal values (≥ 3.5 g/dL)	87	39.55
Decreased values (< 3.5 g/dL)	133	60.45
<i>^b Total lymphocytes</i>		
Normal count (> 1600 /mL)	68	30.91
Decreased count (< 1600 /mL)	152	69.09
<i>^c Total cholesterol</i>		
Normal level (≥ 180 mg/dL)	98	44.55
Decreased level (< 180 mg/dL)	122	55.45
<i>Nutritional status (CONUT score)</i>		
Normal nutritional status (0-1 point)	40	18.18
Light undernutrition (2-4 points)	80	36.36
Moderate undernutrition (5-8 points)	77	35.00
Severe undernutrition (9-12 points)	23	10.45

^a Serum albumin: mean (STD)= 3.24g/dL (0.65 g/dL).

^b Total lymphocytes: mean (STD)= 1457 mL (2448 mL).

^c Total cholesterol: mean (STD)= 175mg/dL (49.1mg/dL).

In accordance with Table IV, the oral examination established that 65% (n=143) of participants were denture

wearers; indeed, 72% (n=103) of them used dentures for more than 5 years.

Oral candidiasis was verified in 28.18% (n=62) of the hospitalized aged patients; the lesions were located in the dorsum of the tongue (41.9%), hard palate (22.5%), lips (16.1%) and other areas (19.3%), including soft palate, gingiva, alveolar ridge, and buccal mucosa.

The most frequent clinical pattern was pseudomembranous candidiasis (64.5%), followed by atrophic erythematous candidiasis (30.6%) and chronic hyperplastic forms (4.8%).

TABLE IV: HOSPITALIZED AGED PATIENTS BY INTRA ORAL VARIABLES. PREVALENCE OF ORAL CANDIDIASIS (N=220).

Variables	n	%
<i>Use of dental prostheses</i>		
No	77	35.00
Yes	143	65.00
<i>Years of use of dental prostheses ^a</i>		
Up to 5 years	40	28.00
> 5 years	103	72.00
<i>Oral candidiasis</i>		
No	158	71.82
Yes	62	28.18
<i>Anatomical areas of oral candidiasis ^b</i>		
Dorsum of tongue	26	41.94
Hard palate	14	22.58
Lips	10	16.13
<i>Clinical pattern of oral candidiasis ^b</i>		
Pseudomembranous candidiasis	40	64.51
Atrophic erythematous candidiasis	19	30.64
Chronic hyperplastic candidiasis	3	4.83

^a Includes only dental prostheses wearing patients.

^b Includes only patients with oral candidiasis.

Finally, Table V shows that the association between oral candidiasis and demographic and intra oral variables was not statistically significant.

Regarding nutritional status, the associations between oral candidiasis in hospitalized aged patients with decreased values of serum albumin (hypoalbuminemia) and severe undernutrition degree were statistically significant ($p=0.009$; $p=0.007$). Thus, OC was more frequently observed in individuals of these groups, being that subjects with hypoalbuminemia showed a 2.3-fold higher chance of developing oral candidiasis (OR=2.3; 95% CI=1.22-4.49) compared to patients with normal albumin levels. Table V shows that patients with severe undernutrition degree exhibited an odds ratio of 0.31 (95% CI=0.12-0.75) compared to a subject with normal nutritional status and light/moderate undernutrition degree.

IV. DISCUSSION

This cross-sectional study showed that 28.1% of the hospitalized older adults presented OC. These findings are slightly different from those reported by others. Indeed, other investigations performed in subjects with similar conditions verified a prevalence ranging between 37-47% [25], [26]. This variation in terms of prevalence may be due to inherent sample characteristics or other methodological differences relative to the diagnosis of oral candidiasis. In the present study, we swabbed only the suggestive area of the mucosa, meanwhile, the results obtained by Wilkieson *et al.* [25] and Paillaud *et al.* [26] could be overestimated because researchers swabbed the fitting surface of a denture and at

least three oral mucosa regions, respectively. Furthermore, it should be noted that the percentage reported in the current study could increase to 35.4% if we included all those cases that presented suggestive clinical lesions but turned out to be negative in the culture analysis and therefore were not considered as OC.

TABLE V: ASSOCIATIONS BETWEEN ORAL CANDIDIASIS AND DEMOGRAPHIC, INTRA ORAL AND NUTRITIONAL STATUS

	With oral candidiasis		Without oral candidiasis		OR (95%CI)	P-value
	n=62	%	n=158	%		
Sex						
Female	31	(50.0)	80	(50.6)	0.97	
Male	31	(50.0)	78	(49.4)	(0.54-1.75)	0.932 ^b
Age groups						
>80 years	35	(56.5)	69	(43.7)	1.67	
65-79 years	27	(43.5)	89	(56.3)	(0.92-3.02)	0.087 ^b
Residence area						
Rural	37	(59.7)	82	(51.9)	1.37	
Urban	25	(40.3)	76	(48.1)	(0.75-2.48)	0.297 ^b
Education						
None / primary	59	(95.2)	138	(87.3)	2.85	
Secondary/ tertiary	3	(04.8)	20	(12.7)	(0.81-9.96)	0.088 ^b
Use of dental prostheses						
Yes	42	(67.7)	101	(63.9)	1.18	
No	20	(32.3)	57	(36.1)	(0.63-2.21)	0.593 ^b
Years of use of dental prostheses						
>5 years	33	(78.6)	70	(69.3)	1.62	
Up to 5 years	9	(21.4)	31	(30.7)	(0.69-3.79)	0.260 ^b
Serum albumin						
Decrease values (<3,5g/dL)	46	(74.2)	87	(55.1)	2.34	
Normal values (≥3,5gr/dL)	16	(25.8)	71	(44.9)	(1.22-4.49)	0.009 ^{a,b}
Total cholesterol						
Decrease level (<180mg/dL)	38	(61.3)	84	(53.2)	1.39	
Normal level (≥180mg/dL)	24	(38.7)	74	(46.8)	(0.76-2.53)	0.275 ^b
Total lymphocytes						
Decrease count (<1600/mL)	44	(71.0)	108	(68.4)	1.13	
Normal count (>1600/mL)	18	(29.0)	50	(31.6)	(0.59-2.15)	0.705 ^b
Nutritional status (CONUT)						
Normal, light, and moderate undernutrition (≤ 8 points)	50	(80.6)	147	(93.0)	0.31	
Severe undernutrition (> 8 points)	12	(19.4)	11	(7.0)	(0.12-0.75)	0.007 ^{a,b}

OR= Odds ratio.

CI= Confidence interval.

^a Significant correlation (≤ 0.05).

^b Chi-square or Fisher's exact test).

CI= Confidence interval.

Respecting nutritional status, it is estimated that hospital undernutrition affects one in two patients at admission, while many others develop undernutrition throughout hospitalization [27]. Our results revealed a considerable prevalence of undernutrition among hospitalized older adults (81.8%) compared to other similar reports [28]. Actually, other authors, have demonstrated undernutrition values range from 19 to 76.6%. This wide range could be explained by the fact that the aforementioned studies used different nutritional

assessment methods [29]-[35]. It should be emphasized that these studies were done in a diverse population with different diet patterns. In summary, the comparison of these results is impracticable because of the lack of a widely accepted nutritional evaluation system.

In a similar study by Paillaud *et al.* [25] patients were nutritionally assessed by evaluation of dietary intake, anthropometric variables including BMI (body mass index), and other anthropometric perimeters. However, there is information asseverating that in an older adult, the BMI is altered due to pathological and physiological changes, including edema and especially those that arise in body composition, such as redistribution from subcutaneous fat in the upper limbs with accumulation in the abdominal region, decrease in height due to vertical shrinkage, among other factors like the collapse of the vertebrae and the curvature of the spine. Thus, estimating BMI in the elderly may lead to inaccurate nutritional status [36]. In the aforementioned study, the patients were also analyzed with biological measurements, such as serum nutritional proteins, albumin, ferritin, Zn, folate, vitamins B12 and C [25].

To provide new information, in the present study we decided to use only biological parameters scored by the CONUT system, which is considered a simple, convenient, useful, accurate, and validated tool for early detection/monitoring of clinical undernutrition and as a predictor of short- and long-term outcomes [37]-[39].

According to Chi-square or Fisher's exact test, our data did not confirm a statistically significant association between OC and demographic/clinical variables. Specifically, concerning the clinical variable dental prostheses use, our findings are interesting since other authors have demonstrated a clear association between these two variables [4]. Despite that in our study most subjects with OC were denture users (67.7%), this association was not statistically significant (p=0.593, OR=1.1). This discrepancy could be explained because the frequent condition of physical and mental deterioration of some older adults, does not allow the constant usage of dental prostheses in the hospital; most of the time, prostheses were stored.

Regarding the association between OC and nutritional variables, our results agree with other investigations showing that the serum albumin levels were significantly different in patients with and without oral candidiasis [2].

The present report revealed a statistically significant association between decreased values of serum albumin (hypoalbuminemia) and OC (p=0.009, OR=2.3). These findings provide further evidence for hypoproteinemia increasing the susceptibility to infections and other complications [40]. In summary, hypoalbuminemia was found to be the best single indicator of allergy and appears to be a predictor of bad prognosis in several different situations [41]. It has been found that albumin increases the vascular endothelial growth factor (VEGF), which directly influences the microvascular integrity, as well as enhances several aspects related to inflammation, including vasodilation, migration of macrophages, and adhesion of neutrophils [42], [43]. Nevertheless, these findings should be interpreted with caution because although serum albumin is a quick manner to determine nutritional status, other conditions are associated

with hypoalbuminemia such as lesions or inflammatory processes [44].

Additionally, some scientific literature argues that hypoalbuminemia should not be considered as an exclusive marker of the degree of undernutrition considering that the half-life of albumin is about 20 days and that, especially in hospitalized elderly patients, the changes in distributional mechanism and albumin metabolism are faster [45]. Instead, pre-albumin or Transthyretin has a much shorter half-life in plasma (2 days) and is more sensitive to reflecting changes in protein-energy status [46], [47]. However, there are conflicting reports on the interpretation of plasma pre-albumin as a potential marker of nutritional status [48]-[50].

Our data also demonstrated that severe undernutrition degree in hospitalized older adults was significantly associated with oral candidiasis ($p=0.007$). This result could be justified because, in the CONUT system, the serum albumin value has a fundamental relevance in the undernutrition assessment. The generalizability of these results is subject to certain limitations. First, we do not consider analyzing pre-albumin as a predictor of undernutrition. Next, patients who were under antibiotic treatment were not excluded which could simultaneously predispose them to oral candidiasis. It is worth mentioning that a nature cross-sectional study does not allow establishing causality in the relationships and associations found. Further studies are warranted to explore the role of undernutrition, specifically hypoalbuminemia, in the development of oral candidiasis.

Conclusions: 28.1 % of the hospitalized aged patients had oral candidiasis. Hypoalbuminemia and severe undernutrition are risk factors associated with oral candidiasis.

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