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Prevalence and Associated Risk Factors of Oral Mucosal Lesions and Orofacial Dyskinesia in Patients with Psychotic Disorders

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Authors' contributions

This work was carried out in collaboration among all authors. Author AAA was involved in the conception of the idea, data collection and drafting of the manuscript. Author FJO was involved in the conception, data analysis and interpretation. Author EOO revised the manuscript for publication. Author BMM participated in study design and assessment of patients with mental disorders. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To determine the prevalence of oral mucosa lesions, facial movement disorders and the associated risk factors among patients with psychotic disorders and controls.
Study Design: A cross sectional study
Place and Duration of Study: The department of mental health and the General outpatients' clinic of the Obafemi Awolowo University Teaching Hospitals Complex, Ile- Ife, Nigeria. between October 2016 to November 2017.
Methodology: One hundred and eighty consenting patients (90 cases and 90 controls) were recruited. Oral mucosa assessment was based on W.H.O guide to epidemiology and diagnosis of oral mucosa diseases. Involuntary facial movement was assessed using the Abnormal Involuntary Movement Scale. Xerostomia assessment was done by volumetric sialometry.
Results: Prevalence of oral mucosa lesions in patients with psychotic disorders was 83.33% while

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it was 71.11% for the controls (P=0.05). The likelihood of developing oral mucosa lesions in patients with psychotic disorders increased with age (Odds ratio 1.02, 95% C.I (1.00-1.03), P=0.04). Orofacial dyskinesia was observed in 17 (18.89%) of the cases on antipsychotic medications and none in the controls (P<0.001). The risk of developing orofacial dyskinesia also increased (Odds Ratio 1.096, 95% C.I (1.03-1.16), P=0.003) with increase in age in the cases.

Conclusion: Oral mucosa lesions and orofacial dyskinesia were more prevalent in patients with psychotic disorders than the controls. Increasing age was a risk factor for developing oral mucosa lesions and orofacial dyskinesia among patients with psychotic disorders.

Keywords: Oral lesions; orofacial dyskinesia; psychotic disorders.

1. INTRODUCTION

Oral health affects the personal, social, and psychological aspects of life [1].Psychosomatic disorders originating from emotional factors are characterized by physical and pathological changes in the body, including the oral cavity [2]. Consequently, a bidirectional relationship exists between mental health and oral health [3]. Oral health conditions that may indicate mental health challenges include burning mouth syndrome [4], self-injurious tendencies [5], halitosis [6] and nocturnal bruxism [7]. Similarly, an association with psychological alteration has been observed in oral mucosa lesions like aphthous stomatitis, oral lichen planus [8] and geographic tongue [9]. High levels of depression and somatization have also been established in patients with chronic orofacial pain conditions [10] and recalcitrant oral mucosa diseases [11].

Treatment of metal health conditions could cause untoward effects that affect the maxillofacial structures. Orofacial dyskinesia, an involuntary repetitive movement of the mouth and face [12] occurs as an adverse effect of long-term exposure to antipsychotic drugs [13]. Antipsychotics are classified into typical or first generation (FGAs) and atypical or second generation (SGAs) [13]. The mode of action of the FGAs is predominantly to act as antagonists at the brain dopamine D_2 receptors [13]. Some associated adverse drug reactions stemming from the mechanism of action includes extrapyramidal motor effects such as acute dystonia, akathisia, parkinsonism, and tardive dyskinesia. However, the mode of action of the SGAs is a predominant antagonism of 5-HT_{2A} receptors with a lesser degree antagonism of dopamine D_2 receptors. Therefore, the SGAs have low or negligible side effects, better effectiveness and supposed increased safety[13]. Other side effects of antipsychotic medications include xerostomia, which could increase risk of caries, oral fungal infections, mucosal lesions, gingivitis and periodontitis [14]. Orofacial dyskinesia is a dreaded disabling condition which runs a chronic course [15]. The long-term effects of orofacial dyskinesia include myalgia of the muscles of mastication, temporomandibular disorders [16], and maxillofacial trauma [17].

Despite the 20% prevalence of mental disorders in the Nigerian population [18],there is a paucity of data relating to the risk factors for oral lesions and orofacial dyskinesia in patients living with mental health challenges. Likewise, the prevalence of oral lesions and orofacial dyskinesia in patients receiving psychiatric care in Nigeria is not fully known. Several oral conditions affect the quality of life of patients with mental disorders. Hence, a need for a study describing oral mucosal lesions in a subset of this group of patients. The attributes and exposure that increases the likelihood of developing such lesions are also worth exploring to ensure a holistic patient management. Furthermore, there is a need to bring these findings to the fore in order to encourage a more robust multidisciplinary approach in the management of patients with mental disorders. This study investigated the prevalence of oral mucosa lesions, facial movement disorders and the associated risk factors among patients diagnosed with psychotic disorders in our environment.

2. MATERIALS AND METHODS

2.1 Ethics

The procedures for this study were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000. Ethical approval for this study was obtained from the ethics and research committee, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife with registration Number: NHREC/27/02/2009a.

2.2 Patients

A cross sectional study with comparison group investigating oral lesions, orofacial dyskinesia and associated risk factors in patients with psychotic disorders attending the mental health clinic of the Obafemi Awolowo University Teaching Hospitals Complex, Ile- Ife, Nigeria and controls from the General outpatients' clinic between October 2016 to November 2017.
The study population comprised of outpatients diagnosed with psychotic disorders. They were randomly selected from the patients being managed in the mental health clinic. Patients were 18 years and above with no co-morbid medical conditions like primary hypertension and diabetes mellitus. The control group was recruited to compare with patients with psychotic disorders. They comprised healthy individuals who visited the general outpatients' department of the hospital on account of routine medical checkup. Other inclusion criteria for control subjects were negative history of diagnosed mental disorder, use of antipsychotic medications and co morbid medical conditions.

2.3 Sample Size Determination

The formula for sample size estimation of two proportions, which gave the total number of sample size required for the two groups, was used. With a statistical significance (Alpha) of 5% and power of 90%, a known prevalence of dyskinesia within the general population was 1.3% [19] and was allotted to population 1 (P1). Also the known prevalence of dyskinesia in patients with mental disorders was 15% [20] and was allotted to population 2 (The comparison group, P2). The effect size (D) of 13.7% (P2-P1) difference was adopted for this study. Attrition rate of 10% (rounded off to 16 patients) was added into the calculated sample size giving a total of 180. Since there are two groups, this translated to 90 patients per group.

2.4 Data Collection

Patients who met the inclusion criteria were informed about the study after which a signed consent was obtained. Biodata such as name, age, sex, address, ethnicity, marital status and occupation were recorded. Information on the patients' past medical history and drug history of note as well as habits that may cause similar oral conditions such as tobacco and alcohol consumption were also recorded in addition to blood pressure and weight. Other relevant information such as established diagnosis of mental disorders and facial movement disorder and the present medication for each participant were obtained from the hospital record.

Detailed extra oral and intraoral examination was done. Oral mucosa assessment was based on the World Health Organization guide to epidemiology and diagnosis of oral mucosal diseases [21].

2.5 Involuntary Facial Movement

Involuntary facial movement was assessed using the Abnormal Involuntary Movement Scale (AIMS) [22]. The scale aids in early detection of dyskinesia and also provides a method for ongoing surveillance. Patients were first observed unobtrusively at rest in the waiting area. Patients were seated on a firm chair without arms for questioning and examination following standard operations as outlined in the scale. Observed abnormal movements of the face and mouth, extremities, trunk and global judgements were rated according to severity on the AIMS scale (0=none, 1=minimal, 2=mild, 3=moderate, 4=severe) by one examiner.

Oral hygiene: Oral hygiene was assessed using Greene and Vermilion's Oral Hygiene Index Simplified [23]. Six teeth were examined one from each sextant (upper anterior right central incisor, upper right first molar, upper left first molar, lower left central incisor, lower right first molar and lower left first molar) of the jaw and the corresponding scores were allotted.

The addition of the total score was divided by the total number of teeth examined (Six). This was done for each of debris and calculus index, respectively. Summation of both debris and calculus index gave the oral hygiene index and was graded: 0-1.2 = good; 1.3-3.0 = fair; 3.1-6.0= poor.

Xerostomia: Assessment of hyposalivation was done by sialometry, measuring resting unstimulated whole saliva using standardized spitting method [24]. Patients were asked to abstain from eating and drinking thirty minutes before saliva collection. Patients were asked to spit into a sputum jar for five minutes. Measurement of the volume of collected saliva was done using a graduated Pasteur pipette. The volume was divided by five minutes to get the flow rate in milliliters/minute (mls/min). Flow rate of 0.3-0.5mls/min was adjudged normal while

rate less than or equal to 0.1mls/min was adjudged hyposalivation [25].

2.6 Examiner Calibration

An initial calibration of the researcher was done by both the supervisor (a consultant mental health physician) and the researcher. The inter-examiner consistency was determined by calculating the Kappa (k) statistics [26]. The Kappa coefficient calculated for this study was 0.91 for oral mucosal lesions and 0.87 for orofacial dyskinesia.

2.7 Mental Health Status of the Comparison Group

Mental health status of the control group was assessed using the General Health Questionnaire 12, GHQ-12 [27]. It has been validated for use in Nigeria [28]. Prospective patients with scores greater than 15, which is indicative of distress were not included in the study.

2.8 Statistical Analysis

Data analysis was done using Stata 13 statistical software (Statacorp, College Station, Texas). Descriptive statistics was used to characterize socio-demographic variables such as age, sex, marital status and occupation. Bivariate analysis such as Chi-square or Fishers' exact test was used as appropriate to compare categorical variables.

The association between the predictors and the outcome was determined using odds ratio for patients with mental disorders with and without the outcome and for the controls and patients with mental disorders. All the risk factors were fitted into a logistic regression model to see how each factor contributed to each of oral lesions and orofacial dyskinesia and the interactions between the factors. Logistic regression was used to determine the role of the predictor and confounders on the primary outcome.

Statistical significance was set at $p<0.05$ and confidence interval was set at 95% for all the analysis.

3. RESULTS

3.1 Distribution of Patients

One hundred and eighty patients participated in this study, 93(51.67%) females and 87(48.33%) males. The controls comprised 49(54.44%) males and 41(45.56%) females with a mean age of 33.30 ($\pm$12.61) years. Overall mean age of patients was 36.68$\pm$12.45 years (Table 1).

3.2 Clinical Characteristics of Patients

Poor oral hygiene was observed in 45(50.00%) of the cases and 20(22.22%) of the controls. Oral lesions were present in 75(83.33%) of the cases and 64(71.11%) of the controls. Orofacial dyskinesia was observed in 17(18.89%) of the cases, while none of the controls had facial movement disorder. Hyposalivation was present in 9(10.00%) of the cases and 1(1.11%) of the controls (Table 1).

The most frequent psychotic disorder was schizophrenia 58(64.44). First generation antipsychotic was used in the management of most of the cases, 77(85.56%). Forty-seven cases (52.00%) were on antimuscarinic (Table 2).

Linear alba buccalis was the most frequent oral mucosa lesion seen in patients with psychotic disorder, 55 out of 90 (61.11%) and the controls 60(66.67%). Other oral lesions include fissured tongue, frictional keratosis and geographic tongue (Table 3).

3.3 Orofacial Dyskinesia in Patients

Table 3 shows orofacial dyskinesia in patients with mental disorders. Orofacial dyskinesia was observed in 17(18.89%) of the cases and none were in the controls. The difference was statistically significant with ($p<0.001$).

3.4 Risk Factor for Oral Lesions and Orofacial Dyskinesia in Psychotic Disorders

Table 4 shows that age is associated with developing oral lesions in mental disorders. This was adjusted for sex, alcohol intake and antipsychotic medication. The likelihood of developing oral lesions increased with every one-year increase in age in patients with psychotic disorders (Odds ratio 1.02, 95% C.I (1.00-1.03), $p=0.04$). Sex, alcohol intake and the type of antipsychotic medication did not have a significant relationship with the likelihood of developing oral lesions.

Another regression model showed that age is associated with developing orofacial dyskinesia

in mental disorders (Table 4). This was adjusted for sex and the type of antipsychotic medication. The risk of developing orofacial dyskinesia increased with age in patients with psychotic disorders (Odds Ratio 1.096, 95% C.I (1.03-1.16), p=0.003).

Table 1. Demographic and Clinical characteristics of patients

Characteristic	Total (N=180)	Cases (N=90)	Controls (N=90)	P value
Age (mean± SD, years)	36.68(±12.45)	40.06(±11.40)	33.30(±12.61)	
Sex (n%)				
Male	87(48.33)	38 (42.44)	49 (54.44)	
Female	93(51.67)	52(57.78)	41(45.56)	
Oral hygiene index simplified (n%)				
Good	69(38.33)	12(13.33)	57(63.33)	
Fair	46(25.56)	33(36.67)	13(14.44)	
Poor	65(36.11)	45(50.00)	20(22.22)	<0.001*
Substance Abuse (n%)				
No	177(98.33)	87(96.67)	90(10.00)	
Yes**	3(1.67)	3(3.33)	0(0.00)	0.25
Alcohol Intake (n%)				
No	175(97.22)	84(93.33)	75(83.33)	
Yes	21(11.67)	6(6.67)	15(16.67)	0.04*
Cigarette Smoking (n%)				
No	175(97.22)	85(94.44)	90(100.00)	
Yes	5(2.78)	5(5.56)	0(0.00)	0.06
Oral lesions (n%)				
Absent	41(22.78)	15(16.67)	26(28.89)	
Present	139(77.22)	75(83.33)	64(71.11)	0.05
Orofacial Dyskinesia (n%)				
Absent	163(90.56)	73(81.11)	90(100.00)	
Present	17(9.44)	17(18.89)	0(0.00)	<0.001*
Hyposalivation(n%)				
Absent	170(94.44)	81(90.00)	89(98.89)	
Present	10(5.56)	9(10.00)	1(1.11)	0.02*

**Statistically significant value (P<0.05), **Cannabis*

Table 2. Clinical diagnosis and findings in the management of cases

Characteristic	N (%)
Mental disorder	
Depression	7 (7.78)
Multiple Psychoactive Substance Use Disorder	1(1.11)
Psychosis	15 (16.67)
Schizophrenia	58 (64.44)
Unspecified Psychotic disorder	4(4.44)
Bipolar Affective Disorder	5(5.56)
Antipsychotics	
First generation	77(85.56)
Second generation	13(14.44)
On antimuscarinic	
Yes	47(52.00)
No	43(48.00)
Duration of mental disorder	

Characteristic	N (%)
6 months	7(7.78)
1-2 years	18(20.00)
3-5 years	65(72.22)

Table 3. Oral lesions and dyskinesia in patients with mental disorders and controls

Oral lesions	Case (N=90)	Controls (N=90)	*P* value
Fissured tongue (n%)			
Absent	71(78.89)	87(96.67)	
Present	19(21.11)	3(3.33)	<0.001*
Frictional keratosis (n%)			
Absent	80(88.89)	87(96.67)	
Present	10(11.11)	3(3.33)	0.08
Linea alba (n%)			
Absent	35(38.89)	30(33.33)	
Present	55(61.11)	60(66.67)	0.44
Geographic tongue (n%)			
Absent	87(96.67)	90(100.00)	
Present	3(3.33)	0(0.00)	0.25
Orofacial dyskinesia (n%)			
Absent	73(81.11)	90(100.00)	
Present	17(18.89)	0(0.00)	<0.001*

**Statistically significant value (P<0.05)*

Table 4. Risk factors for oral lesions and orofacial dyskinesia in psychotic disorders

Risk facator	Odds ratio	95% Confidence interval	P value
For Oral Lesions	1.02	1.00-1.03	0.04*
Age (Years)			
Males (Reference Females)	1.81	0.87-3.77	0.11
Alcohol Intake(yes)	0.38	0.12-1.28	0.12
Antipsychotic:1st generation(Reference 2nd generation)	1.22	0.42-3.54	0.72
For Orofacial dyskinesia			
Age (years)	1.096	1.03-1.16	0.003*
Male (Reference Female)	1.71	0.53-5.55	0.37
Antipsychotic type:1st generation (Reference 2nd generation)	0.14	0.02-1.81	0.07

**Statistically significant value (P<0.05)*

Table 5. Antipsychotics as a risk factor for orofacial dyskinesia

Antipsychotic	Orofacial dyskinesia absent (n%)	Orofacial dyskinesia present (n%)	*P* value
First Generation	62(80.52)	15(19.48)	
Second Generation	11(84.62)	2(15.38)	
Not on antipsychotic	90(100.00)	0(0.00)	
Total	163(90.56)	17(9.44)	<0.001*

*Fisher's exact, *statistically significant*

3.5 Antipsychotics and Orofacial Dyskinesia

Table 5 shows that the type of antipsychotics is a risk factor for orofacial dyskinesia in patients with mental disorders. Orofacial dyskinesia was observed in 15(19.48%) cases on first generation antipsychotics while 2(15.38%) cases on second generation antipsychotics had orofacial dyskinesia. The observed difference was statistically significant with $p<0.001$.

4. DISCUSSION

Oral lesions with psychosomatic etiology are still not a sufficiently explained subgroup of diseases, which have long been known in medicine [29].They occur in response to neurotransmitter imbalance in the brain and somatization of oral complaints due to impaired cognitive processes in the higher centers of the brain [8]. Psychological alterations establish its impact on the body, including the oral cavity, by the multidirectional and close interrelations among the nervous, immune and endocrine systems [30].

Some studies from South Asia have previously documented oral lesions in patients with mental disorders. We observed a much higher prevalence than the 39.3% reported by Arjun and colleagues in that region [31]. There is a marked difference in the specific oral lesions reported in their study. While linea alba buccalis and fissured tongue had the highest proportion in this study, leukoplakia and oral submucous fibrosis were the most prevalent oral lesions observed by Arjun and colleagues. This can be attributed to high tobacco and areca nut consumption among the patients with mental disorders in their study population. In contrast, the prevalence of tobacco smoking in patients with psychotic disorders in our study was lower at 5.56%.

Linea alba is a common asymptomatic alteration of the buccal mucosa [32]. This may explain the high proportion in both the cases and the control in this study. Fissured tongue is relatively less common, and it is characterized by presence of grooves or fissures on the dorsum or lateral surface of the tongue [33]. The etiology remains unclear however, associations with genetics and systemic diseases such as psoriasis, diabetes and orofacial granulomatosis have been reported [34]. In males, fissured tongue and geographic tongue may be a significant predictor for burning mouth sensation [35]. The etiology of geographic tongue is unknown however, risk factors associated with mental health such as stress have been implicated and the disorder may be accompanied by anxiety [9].

In another similar study by Dangore and colleagues [36], a lower prevalence of 45.3% for oral lesions among individuals with mental disorders was reported. Recurrent aphthous stomatitis, burning mouth syndrome and oral lichen planus were observed more commonly in their study. Differences in sociocultural and environmental factors may have been responsible for the markedly different observation in the specific oral lesions in our study compared with other similar studies. Their study was carried out among an Indian population, with a high prevalence of tobacco use in different forms, chewing of areca nuts and other agents.

A few risk factors have been identified for oral lesions in individuals with mental disorders. These risk factors are largely life style and habit related. They include tobacco smoking ,alcohol intake, among others [31]. This study showed an association between an increase in age and development of oral lesions in individuals with psychotic disorders compared to the controls.

Suresh and colleagues [8] and Arjun and colleagues [31] reported a prevalence of 5.17% and 30.30% respectively for oral lesions in patients who have not been diagnosed with any mental disorders in studies that compared oral lesions in individuals with mental disorders and controls. These values are, however, at variance with the recorded prevalence in this study. Marked aforementioned differences were also observed in specific oral lesions like in the mental health population and similar sociocultural and environmental factors may be responsible.

A Nigerian study reported a prevalence of 27% for tardive dyskinesia in patients with mental health challenges [37]. The higher prevalence may be because of the study considering both orofacial and appendicular dyskinesia as a sub syndrome of tardive dyskinesia. Furthermore, a systematic review by Correll and colleagues reported 32.4% and 13.1% prevalence for adults on first generation and second generation antipsychotic respectively [38]. It is noteworthy that most of the literature on dyskinesia did not consider orofacial dyskinesia in isolation, but as a sub syndrome of tardive dyskinesia. In addition, a common denominator observed in

patients in this study and other literature that reported tardive dyskinesia is that drugs (antipsychotics and neuroleptics) are a common risk factor [39]. Therefore, the association between the generations of antipsychotics and orofacial dyskinesia observed in this study is consistent with findings in the literature [38].

Dyskinesia is still a major concern in psychiatry. It is most often a side effect of psychotropic drugs, especially the first generation antipsychotics [40].Although the prevalence is decreasing with the advent of second-generation antipsychotics [41], most psychiatric care receivers in resource limited environment like Nigeria are still treated with the first generation psychotropic drugs because the second-generation drugs are more expensive. In addition, the limited coverage of health insurance compels many patients to pay out of pocket for the more affordable first-generation drugs. Similar to first generation antipsychotics, the atypical antipsychotics have some degree of D2 antagonism but more of a blockade of 5HT2A receptors [42]. Loose binding to and fast dissociation from D2 receptors is suggested to cause their lower propensity for dyskinesia [43]. All the patients in this study with orofacial dyskinesia did not experience any existing movement disorder prior to the commencement of psychotropic medications.

This study showed an association between increasing age and the development of orofacial dyskinesia in individuals with mental disorders. This is consistent with findings in other studies wherein ageing was observed as a critical factor in developing dyskinesia [44]. The explanations that have been suggested that associate age with dyskinesia are increased incidence of medical illness with advancing age and neurochemical changes [45].Matson and colleagues suggested decrease in drug metabolism capacity with advancing age as a risk factor for dyskinesia [44]. Other reported non-modifiable risk factors not observed in this study are female sex, race and duration of mental disorder [46].

Although mental health caregivers may not diagnose oral lesions, their presence in this group of patients calls for a good understanding of the interaction between oral health and mental health. The lack of coordination between oral physicians and psychiatrists is evident by the few referrals between the two specialists in the center in which this study was carried out. Although the oral lesions and dyskinesia observed at the time this study was carried out were mostly not symptomatic, long-term effects may require patient follow up.

5. CONCLUSION

The prevalence of oral lesions present in patients with psychotic disorders was higher than in the controls from the same base. Fissured tongue, frictional keratosis, linea alba and geographic tongue were the oral mucosal lesions seen in both cases and control. However, only the presence of fissured tongue was statistically significant in both groups.

Increasing age was a risk factor for developing oral lesions and orofacial dyskinesia in patients with psychotic disorders. Treatments with first generation antipsychotics were more associated with orofacial dyskinesia than second-generation antipsychotics.

To further establish causality between psychotic disorders and oral lesions, an experimental study is recommended. Moreover, interprofessional collaboration between mental and oral health physicians can be strengthened by the provision of an avenue for more knowledge, insights, and resource sharing. This partnership will enhance the understanding of professional roles with a view of a more holistic approach to patient management.

6. LIMITATIONS OF THE STUDY

This study did not quantify the extent to which oral lesions and orofacial dyskinesia exacerbates the mental disorders of the patients. Being a cross sectional study, it cannot lend to discussions on causation.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

All authors declare that written informed consent was obtained from all the patients that participated in this study. A copy of the form is available to the editorial board of this journal.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the ethics and research committee, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife with registration Number: NHREC/27/02/2009a.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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