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ORIGINAL ARTICLE

# Recurrent Salivary Gland Infections in Covid-19

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## Abstract

**Background** SARS-CoV-2 has been shown to infect salivary glands, and post-infectious inflammatory repair may contribute to salivary hyposecretion.

**Objective** To evaluate the recurrence rate of acute salivary gland infections in post–COVID-19 patients using clinical, radiological, and microbiological parameters.

**Methods** A prospective case–control study was conducted at the Otolaryngology Department, Faculty of Medicine, Benha University, from June to December 2023. Sixty patients were enrolled and divided into two groups: Group A included 30 post–COVID-19 patients, and Group B comprised 30 age- and gender-matched individuals without prior COVID-19 infection. After excluding patients lost to follow-up, 26 patients remained in Group A (mean age: 40.13 ± 13.48 years) and 27 in Group B (mean age: 40.50 ± 13.01 years).

**Results** No statistically significant differences were observed between groups regarding microbial variability ($p = 0.679$), recurrence rates of salivary gland infections ($p = 0.075$), or disease-free intervals ($p = 0.063$).

**Conclusions** Post–COVID-19 status was not associated with increased recurrence of acute salivary gland infections, and the microbial profile remained consistent with typical acute presentations. Further research is warranted to explore the potential link between SARS-CoV-2 and chronic sialadenitis.

**Trail Registry** Study protocol registered at *clinicaltrial.gov* Identifier: NCT05890547.

**Keywords** Coronavirus disease 2019 (COVID-19) · Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) · Infectious diseases · Oral manifestations · Sialadenitis

## Background

Seven coronaviruses currently known to infect humans belong to types α and β. Both HCoV-229E and HCoV-NL63 belong to type α. HCoV-OC43, CoV-HKU1, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), and 2019 novel coronavirus (2019-nCoV), belong to type β. CoV-HKU1, SARS-CoV, MERS-CoV, and 2019-nCoV can cause human pneumonia [1].

Saliva can host several viruses including SARS-CoV-2 [2]. The spike protein receptor binding domain (RBD) of 2019-nCoV can bind to the ACE2 receptor on the host cells completing its adsorption. Therefore, cells with ACE2 receptor distribution are host cells for 2019-nCoV and cause inflammatory reactions in these organs [3, 4].

Liu et al. [5] demonstrated, via immunohistochemistry in Chinese rhesus macaques, the presence of ACE2 receptors in the epithelial cells of salivary gland ducts. In humans, ACE2 protein is expressed in salivary glands at a mean level of 1.8 pTPM, ranking 10th among all organs and exceeding expression in lung tissue. These receptors are considered early targets for SARS-CoV infection.

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Repair mechanisms of post-inflammatory damage by fibroblast proliferation and fibrous connective tissue formation [6]. Fibrous repair of acinar cell damage leads to salivary gland hyposecretion, and stenosis in these ducts with subsequent hyposecretion of salivary glands reducing salivary flow [7].

Hyposecretion affects the salivary ductal system flushing, increasing the probability of retrograde infection from ductal orifices [8]. Also, increases the possibility of deposition of inorganic salts on the ductal wall, causing sialolithiasis [9, 10].

These reparative changes may contribute to the development of chronic obstructive sialadenitis, which is hypothesized to be associated with 2019-nCoV infection [6].

According to the National Institute for Health and Care Excellence (NICE), post–COVID-19 syndrome is defined as the persistence of signs and symptoms beyond 12 weeks following acute infection, without an alternative clinical explanation [11].

## Objectives

To determine the recurrence rate of acute salivary gland infections in post–COVID-19 patients based on clinical, radiological, and microbiological findings.

### Patients and Methods

A prospective observational (Case–Control) study of 60 patients allocated into 2 groups at the Otolaryngology Department, Faculty of Medicine, (YYYY) University during the duration from June 2023 to December 2023. This study was approved by (XXX) Faculty of Medicine's ethical committee (REC-FOMBU), Egypt, which approved the study protocol with the approval number RC 21-4-2023. A written informed consent form was obtained from all patients in this study. Study protocol registered at *clinicaltrial.gov* Identifier: NCT05890547.

Adult individuals aged 18 years and older were included as post–COVID-19 patients if they had confirmed infection based on a positive PCR test, characteristic chest CT findings, and positive serological results. Typical CT features included non-systematic ground-glass opacities with a predominantly subpleural distribution, and in later stages, alveolar condensation without evidence of excavation, nodules, or masses. Data related to the acute phase of COVID-19 were collected retrospectively through a detailed review of medical records, conducted in the presence of the patient to enhance accuracy. Information regarding salivary gland infection history prior to COVID-19 was obtained during the enrollment phase.

COVID-19 severity was classified according to the WHO Clinical Progression Scale [12], which categorizes patients based on clinical status, ranging from mild (ambulatory with no limitation of activities) to severe (requiring oxygen therapy, mechanical ventilation, or intensive care). This classification was applied using documented symptoms, hospitalization records, and clinical assessments available in patients' files.

Patients were excluded if they had severe SARS-CoV-2 infection or clinical signs of severe COVID-19, autoimmune diseases, a history of head and neck cancer, prior radiotherapy and/or chemotherapy for head and neck malignancies, facial nerve palsy, chronic sialadenitis, sialolithiasis, or a history of oral surgery.

**Group A** comprised 30 post–COVID-19 patients with confirmed SARS-CoV-2 infection, diagnosed by a positive nasopharyngeal swab using real-time reverse transcription polymerase chain reaction (RT-PCR), accompanied by characteristic clinical symptoms and radiological findings consistent with COVID-19.

**Group B** comprised 30 individuals matched to the study group by age, gender, and chronic comorbidities such as diabetes mellitus and hypertension. These participants had no evidence of prior COVID-19 infection, confirmed by negative nasopharyngeal swab results and absence of clinical symptoms or radiological findings consistent with SARS-CoV-2.

All patients in this study submitted to full ENT and intraoral, head, and neck clinical examination. Careful inspection of the head and neck. The sequence used in performing the head and neck examination was done for all patients including inspection of the face and head and neck region for asymmetry or redness, swelling, or fistulas if present followed by palpation for tenderness or any palpable cervical nodes, also systematic palpation of major salivary glands using a bilateral technique.

A thorough inspection of intraoral structures—including the tongue, oropharynx, teeth, gingiva, lingual frenum, sublingual folds, and sublingual caruncle (housing the openings of Wharton's ducts)—was performed using a tongue depressor and dental mirror. This was followed by bi-digital palpation of the lips, buccal mucosa, and hard palate, and bimanual palpation of the floor of the mouth and submandibular glands. The latter was conducted by placing the index finger intraorally and supporting it externally with the fingers of the opposite hand, allowing gentle compression and assessment of the intervening tissues.

Following comprehensive inspection and palpation, all observations concerning the size, shape, consistency, location, and surface characteristics of the affected salivary glands were documented in the patient's clinical record.

All patients underwent neck ultrasonography with Doppler imaging to evaluate gland dimensions, detect possible abscess formation, and exclude vascular anomalies that may complicate the differential diagnosis of submandibular swellings. This imaging approach highlights the diagnostic challenges and complexities in managing salivary gland infections. Radiological assessments for all patients were performed by a single operator † using the LOGIQ P10 ultrasound system (Serial No: LPZ440205). A superficial probe was employed for neck examinations, utilizing frequencies L3_L2 or M16_15.

Biopsy procedures were performed based on clinical indications to establish a definitive diagnosis in cases of suspected tumors or highly suspicious masses. Specifically, incisional biopsy was conducted in one patient from Group A, needle core biopsy in five patients (two in Group A and three in Group B), and excisional biopsy in one patient from Group A. These procedures were documented in the clinical records and guided by the presenting scenario [13].

Groups were compared based on patient characteristics, risk factors, etiological factors, clinical symptoms, and the occurrence or recurrence of acute sialadenitis. Recurrence was defined as the reappearance of clinical signs and symptoms indicative of salivary gland infection or inflammation at least four weeks following resolution of the initial episode. This definition was supported by clinical documentation and patient follow-up records. Acute sialadenitis was diagnosed based on hallmark clinical features, including discomfort, swelling, and pain in the major salivary glands (parotid and submandibular), along with purulent discharge from the duct orifice.

Causative organisms were identified from specimens collected via swabs or pus aspiration at the time of primary clinical presentation. Samples were first subjected to direct Gram staining (Oxoid, UK), followed by inoculation onto nutrient, blood, chocolate, and MacConkey agar plates (Oxoid, UK) using the streak plate method. All cultures were incubated aerobically and anaerobically at 37°C for 24–48 h. In cases of mixed microbial growth, subculturing was performed on the same media types to isolate individual colonies. Identification of organisms was based on Gram stain morphology, hemolysis patterns on blood agar, and standard biochemical tests including catalase, coagulase, and oxidase assays (Oxoid, UK)[14].

All assessments—clinical, microbiological, and radiological—were performed by the same designated examiner for each domain to ensure procedural consistency and reduce inter-observer variability.

## Statistical Analysis of the Data

Data was analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Statistical significance was assessed at the 5% level ($p<0.05$). Missing data was not imputed and were excluded from the relevant analyses.

The study sample size was estimated a priori using G*Power software version 3.1.9.7 (Heinrich-Heine-University, Düsseldorf, Germany). Although the Gherlone cohort (2019) does not report recurrence rates of salivary gland infections, it documents a high prevalence of post–COVID-19 salivary dysfunction, including salivary gland ectasia (≈38–43%) and xerostomia (≈30%). These findings provide biological justification for anticipating a moderate-to-large increase in infection recurrence risk, though not used as direct input for proportion estimates. Assuming a 20% absolute difference in recurrence rates between groups (e.g., 20% vs. 40%), a sample size of approximately 60 patients per group would provide 80% power, while 80 patients per group would yield 90% power. The calculation was based on a two-tailed test with $\alpha=0.05$ using the following equation:

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}$$

where $n'$ = Sample size with finite population correction,

$N$ = Population size,

$Z$ = Z statistic for a level of confidence,

$P$ = Expected proportion (If the prevalence is 20%, $P=0.2$), and

$d$ = Precision (If the precision is 5%, then $d=0.05$).

Following data collection, a post hoc power analysis was conducted for the primary outcome—recurrence of salivary gland infections in post–COVID-19 versus control patients. The study included 26 post–COVID-19 patients and 27 controls. Based on the observed recurrence rates (Table 5) and the between-group difference ($p=0.075$, two-sided), the achieved statistical power was approximately 63% at a significance level of $\alpha=0.05$. This relatively low power reflects the limited sample size, which reduces the ability to detect moderate effect sizes with conventional thresholds. As post hoc power is mathematically linked to the observed p-value and effect size, it reinforces the interpretation that the study was underpowered to definitively confirm or exclude a statistically significant difference at the conventional 80% power threshold [15, 16].

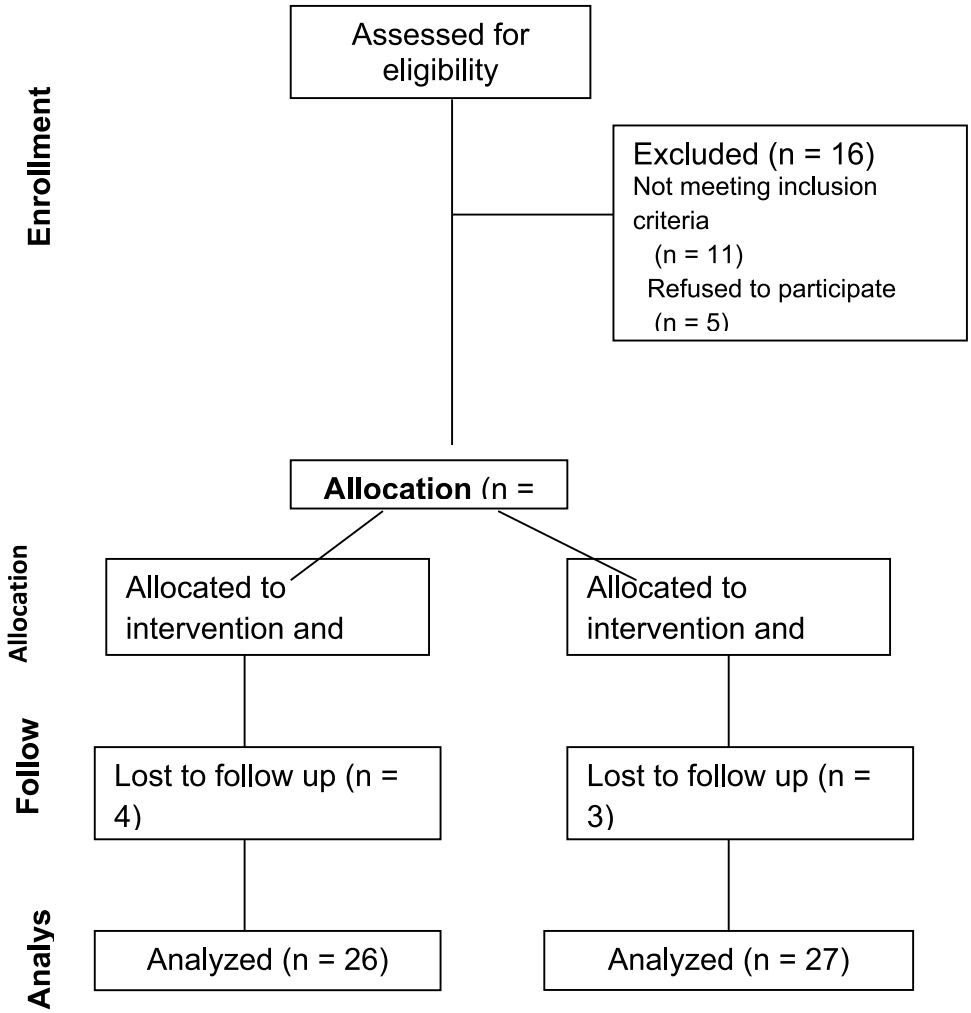


**Fig. 1** CONSORT diagram showing the flow of participants through each stage of the study

**Table 1** Age and gender throughout both groups

| | Group A (n = 26) | Group B (n = 27) | *p-value* |
|---|---|---|---|
| Gender | | | |
| Male | 13 (50.0%) | 11 (40.7%) | 0.498 |
| Female | 13 (50.0%) | 16 (59.3%) | |
| Age | | | |
| 18 -50 yrs | 20 (76.9%) | 21 (77.8%) | 0.941 |
| > 50 yrs | 6 (23.1%) | 6 (22.2%) | |
| Mean ± SD | 40.13 ± 13.48 | 40.50 ± 13.01 | 0.915 |

*SD* Standard deviation, *t* Student t-test, $\chi^2$ Chi-square test, *MC* Monte Carlo, *p* p-value

## Results

A total of 76 patients were assessed for eligibility. Sixteen were excluded, 11 for not meeting inclusion criteria and 5 who declined participation. The remaining 60 eligible patients were enrolled and allocated into two groups. Seven patients (four in Group A and three in Group B) were lost to follow-up during the study period and did not complete the scheduled evaluations. As a result, they were excluded from the final analysis. This has been noted in the Results section and illustrated in Fig. 1.

Table 1 shows patients' demographic data. After patients dropped out group (A) included 26 patients (13 males and 13 females) with a mean age of 40.13 ± 13.48 years while group (B) 27 patients (11 males and 16 females) with a mean age of 40.50 ± 13.01 years without statistical difference between both groups regarding age and gender.

There is no statistical difference between studied patients across both groups regarding risk factors including diabetes mellitus, systemic hypertension, smoking, hepatitis, and steroid medication usage Table 2.

Patients' clinical manifestations such as fever, dryness of mouth, and major salivary gland swelling show no statistical difference between groups Table 3.

No histopathological evidence of malignancy was identified in any of the biopsy specimens obtained from patients in either study group.

Causative organisms from collected cultures showed no statistical difference between groups as studied through either swabs or aspiration of pus at the primary time of

**Table 2** Patients' risk factors throughout both groups

| Risk factors | Group A (n=26) | Group B (n=27) | *p-value* |
|---|---|---|---|
| Smoking | 6 (23.1%) | 7 (25.9%) | 0.810 |
| DM | 8 (30.8%) | 7 (25.9%) | 0.696 |
| Hypertension | 9 (34.6%) | 12 (44.4%) | 0.465 |
| Hepatitis | | | |
| No | 21 (80.8%) | 22 (81.5%) | $^{MC}$p=0.469 |
| B | 2 (7.7%) | 0 (0.0%) | |
| C | 3 (11.5%) | 5 (18.5%) | |
| Steroid medications | 11 (42.3%) | 11 (40.7%) | 0.908 |

*SD* standard deviation, *t* Student t-test, $\chi^2$ Chi-square test, *MC* Monte Carlo, *p* p-value

**Table 3** Patients' clinical manifestations in both groups

| Patients' clinical manifestations | Group A (n=26) | Group B (n=27) | *p-value* |
|---|---|---|---|
| Temperature rise | | | |
| Fever | 8 (30.8%) | 8 (29.6%) | $^{MC}$p=1.000 |
| Mild fever | 3 (11.5%) | 3 (11.1%) | |
| High fever | 15 (57.7%) | 16 (59.3%) | |
| Dryness of mouth | 6 (23.1%) | 9 (33.3%) | 0.407 |
| Swelling | | | |
| Right submandibular | 11 (42.3%) | 13 (48.1%) | $^{MC}$p=0.980 |
| Left submandibular | 8 (30.8%) | 8 (29.6%) | |
| Right parotid | 3 (11.5%) | 3 (11.1%) | |
| Left parotid | 2 (7.7%) | 1 (3.7%) | |
| Bilateral submandibular | 1 (3.8%) | 0 (0.0%) | |
| Bilateral parotid | 1 (3.8%) | 2 (7.4%) | |

*SD* standard deviation, *t* student t-test, $\chi^2$ Chi-square test, *MC* Monte Carlo, *p* p-value

**Table 4** Causative organism of salivary gland infection in both groups at primary time of presentation

| Or pharyngeal swab/ causative organism | Group A (n=26) | Group B (n=27) | *p-value* |
|---|---|---|---|
| No bacterial growth | 8 (30.8%) | 9 (33.3%) | $^{MC}$p=0.679 |
| Staph aurues | 10 (38.5%) | 11 (40.7%) | |
| *Moraxella catarrahlis* | 2 (7.7%) | 0 (0.0%) | |
| Mixed infection (streptococci viridans+ananaerobes) | 5(19.2%) | 7(25.9%) | |
| Mixed infection (Gram-negative *E. coli*+anaerobes) | 1(3.8%) | 0 (0.0%) | |

*SD* standard deviation, *t* student t-test, $\chi^2$ chi-square test, *MC* Monte Carlo, *p* p-value

**Table 5** Comparison between the two studied groups according to recurrence

| Recurrence | Group A (n=26) | Group B (n=27) | *p-value* |
|---|---|---|---|
| No | 11 (42.3%) | 18 (66.7%) | 0.075 |
| Yes | 15 (57.7%) | 9 (33.3%) | |

$\chi^2$ Chi-square test, *p* p-value

**Table 6** Kaplan–Meier survival curve for disease-free survival

| | Mean | % End of study | Log-rank | |
|---|---|---|---|---|
| | | | $\chi^2$ | *p-value* |
| Group A | 4.423 | 42.3 | 3.450 | 0.063 |
| Group B | 5.185 | 66.7 | | |

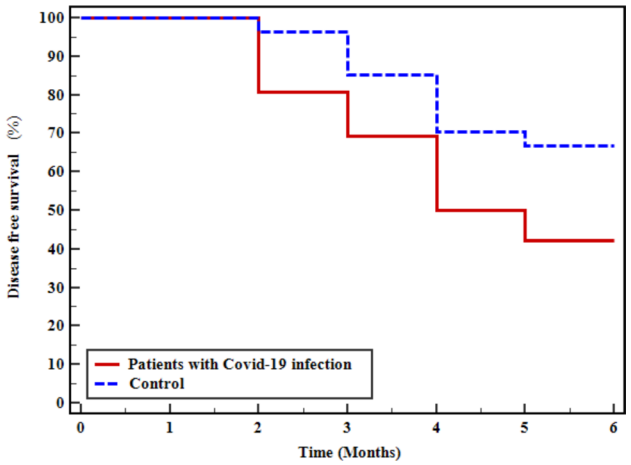


**Fig. 2** Kaplan–Meier survival curve for disease-free survival

presentation (*p-value*=0.679) with a predominance of S.auris as the main bacterial pathogen detected in both groups as shown in Table 4. There is no change in the variability of the causative micro-organisms causing acute salivary infection.

Recurrence of salivary gland infections was not significantly higher in Group A compared to the control Group B (p=0.075), as shown in Table 5. Similarly, no statistically significant difference in the disease-free interval was observed between the study and control groups (p=0.063), as detailed in Table 6 and illustrated in Fig. 2.

The multivariate Cox regression model was used to assess the impact of COVID-19 infection and various clinical risk factors on the recurrence of salivary gland infections. Although none of the variables reached conventional statistical significance (p<0.05), several findings suggest clinically relevant trends:

- **COVID-19 infection:** Patients with prior COVID-19 infection showed a hazard ratio (HR) of 2.220 (95% CI: 0.935–5.270; p=0.071), indicating a more than twofold increased risk of recurrence. While not statistically significant, this borderline result suggests a potential association that warrants further investigation in larger cohorts.
- **Smoking:** HR=1.427 (p=0.446) suggests a modest increase in recurrence risk, though the wide confidence interval (0.572–3.561) and lack of significance limit interpretability. • Hypertension: HR=1.884 (p=0.317)

**Table 7** Multivariate analysis COX regression analysis for the parameters affecting Recurrence

| | B | SE | Sig | HR | 95% CI | |
|---|---|---|---|---|---|---|
| | | | | | LL | UL |
| Patients with Covid-19 infection | 0.797 | 0.441 | 0.071 | 2.220 | 0.935 | 5.270 |
| Risk factors | | | | | | |
| Smoking | 0.356 | 0.466 | 0.446 | 1.427 | 0.572 | 3.561 |
| DM | −0.318 | 0.649 | 0.624 | 0.727 | 0.204 | 2.597 |
| Hypertension | 0.633 | 0.633 | 0.317 | 1.884 | 0.545 | 6.507 |
| Hepatitis | −0.058 | 0.541 | 0.915 | 0.944 | 0.327 | 2.724 |
| Steroid medications | 0.073 | 0.509 | 0.886 | 1.076 | 0.397 | 2.916 |

*HR* hazard ratio, *SE* estimates standard error, *B* unstandardized coefficients (linear regression), *C.I* confidence interval, *LL* lower limit, *UL* upper limit

also indicates a possible elevated risk, but again, the result is not statistically conclusive.

- **Diabetes mellitus, hepatitis, and steroid use:** These factors showed HRs below or near 1, with wide confidence intervals and non-significant p-values, suggesting no strong independent association with recurrence in this sample.

Overall, the model highlights COVID-19 infection as the most prominent variable with a potential effect on recurrence, though the study may be underpowered to detect definitive associations. These findings should be interpreted cautiously and validated in future studies with larger sample sizes and longer follow-up durations. Table 7

## Discussion

Several case reports and small series have documented oral cavity abnormalities in patients with COVID-19, including salivary gland involvement [16]. Liu et al. [5] further demonstrated that salivary gland epithelial cells can be infected in vivo shortly after SARS-CoV-2 exposure, serving as a significant source of viral shedding in saliva during the early phase of infection. These findings underscore the biological plausibility of salivary gland dysfunction in COVID-19 and support the rationale for investigating both acute and post-infectious glandular manifestations.

Minor salivary glands exhibit higher ACE-2 expression than lung tissue, making them a potential reservoir for SARS-CoV-2. Viral detection in saliva can reach up to 92% [17], and both SARS-CoV and SARS-CoV-2 have been linked to acute and chronic sialadenitis [6].

Dry mouth has been reported more frequently in COVID-19 patients [18]. This may be attributed to two mechanisms: reduced salivary secretion compromises the integrity of oral mucosal barriers, facilitating viral colonization and adhesion; and diminished salivary flow impairs the release of antimicrobial peptides and proteins essential for oral immune defense [19, 20].

Gherlone et al. [16] reported salivary gland ectasia as the most prevalent oral manifestation in post–COVID-19 patients, observed in 38% of cases, with a significant male predominance and association with older age and more severe COVID-19 presentations. Additionally, diabetes mellitus and chronic obstructive pulmonary disease (COPD) were significantly linked to xerostomia. In contrast, our study did not identify a statistically significant association between post–COVID-19 status and salivary gland recurrence, nor between recurrence and the risk factors, suggesting that glandular involvement may vary across populations and clinical settings.

Our study demonstrated that clinical manifestations—including fever, xerostomia, and major salivary gland swelling—did not differ significantly between post–COVID-19 patients and the control group. This suggests that these symptoms may not be uniquely attributable to prior SARS-CoV-2 infection in the context of recurrent acute salivary gland infections. The lack of statistical difference across both groups indicates that such clinical features remain consistent with typical presentations of salivary gland infections, regardless of COVID-19 history. These findings further support the notion that post-infectious glandular involvement may be transient and not necessarily associated with distinct clinical patterns.

The current study does not support the findings of Gherlone et al. [16], as no statistically significant differences were observed between groups in terms of age, gender, or key risk factors. Specifically, diabetes mellitus ($p=0.696$), systemic hypertension ($p=0.465$), smoking ($p=0.810$), hepatitis ($p=0.469$), and steroid medication use ($p=0.908$) showed no meaningful association with recurrence in our cohort.

There was no statistical difference between both groups regarding causative organisms as studied through either swab or from collected cultures at the time of presentation (*p-value*$=0.679$) with a predominance of S.auris as the main bacterial pathogen detected in both groups accounting for 38.5% in group (A) and 40.7% in group (B). There is no change in the variability of the causative micro-organisms

causing acute salivary infections. These results match Brook et al. [21], Raad et al. [22], and Danstrupet al [23] results.

No bacterial growth was found in collected cultures accounting for 30.8% in group (A) and 33.3% in group (B) with no statistical difference between both groups (*p-value* = 0.679), viral etiology might be in question in those percentages of patients.

The current study showed no statistically significant higher recurrence of salivary gland infections in group (A) than in control group (B) (*p-value* = 0.075) without significant disease-free interval compared to the control group (*p-value* = 0.063).

Although Brandini et al. [24] suggest that oral lesions in SARS-CoV-2 patients may result from systemic immune dysregulation and opportunistic coinfections—particularly during hospitalization—we do not fully support extrapolating this explanation to the recurrence of salivary gland infections in post–COVID-19 patients. Our findings did not demonstrate a higher recurrence rate or significant microbial variability and therefore do not align with the proposed mechanism of immune compromise and opportunistic infection as a primary driver in this context.

The observed outcomes may be better explained by transient glandular dysfunction or localized inflammation during acute SARS-CoV-2 infection, rather than persistent immune dysregulation or opportunistic coinfection. The consistent microbial profile further suggests that any recurrence likely follows typical etiological patterns, not post-viral immunosuppression.

This study was designed to assess the recurrence of acute salivary gland infections in post–COVID-19 patients. Due to methodological and temporal limitations, the chronic nature of salivary gland involvement could not be evaluated. This remains an open question, and further longitudinal studies are warranted to elucidate the potential development of chronic sialadenitis following SARS-CoV-2 infection.

## Conclusion

No significant increase in recurrent acute salivary gland infections was observed among post–COVID-19 patients, nor was there notable variation in the causative microorganisms during the acute phase. Given the observational nature of the study, these findings suggest association rather than causation. Further research is warranted to clarify the potential link between SARS-CoV-2 and chronic sialadenitis.

### Limitations

This study has several limitations. Functional assessment of major salivary glands was feasible due to facility constraints, and the role of minor salivary glands in the observed clinical condition remains unexplored. The small sample size limits generalizability. Retrospective data on pre–COVID-19 salivary gland disorders and oral infections may introduce bias, and accurate records of hospital admission and length of stay were unavailable. Lastly, while a potential link between antibiotic use and salivary gland ectasia suggests involvement of the salivary microbiome, this association could not be directly confirmed.

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**Author Contributions** The authors confirm their contribution to the study and article as follows: AFG, RFT and EFA; study idea and design. RFT; data collection, draft manuscript preparation. RAE; microbiological assessment of samples. EFA; clinical assessment, data analysis and interpretation of results. All authors reviewed the results and approved the final version of the manuscript. The corresponding author confirms that the manuscript has been read and approved for submission by all the named authors. The requirements for authorship as stated have been met, and each author believes that the manuscript represents honest work.

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**Data Availability** The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Declarations

**Conflict of Interest** The authors declare no conflict of interest.

**Ethical Approval and Informed Consent** This study was approved by the Benha Faculty of Medicine's ethical committee (REC-FOMBU), Egypt, which approved the study protocol with the approval number RC 21–4-2023. The study was carried out in compliance with the Helsinki Declaration of 1975 and its amendments. A written informed consent form was obtained.

**Consent for Publication** All authors of this research confirm their consent for publcation of this study.

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