IDR International Dental Research

Int Dent Res 2023; 13(3): 119-24
https://doi.org/10.5577/intdentres.492

Original Article Open Access

Evaluation of gingival crevicular fluid volume with periopapers in patients who have recovered from COVID-19 infections

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Received: 25 September 2023
Accepted: 16 November 2023

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How to cite this article:

Üner DD, İzol BS. Evaluation of gingival crevicular fluid volume with periopapers in patients who have recovered from COVID-19 infections. Int Dent Res 2023;13(3):119-24. https://doi.org/10.5577/intdentres.492

Abstract

Aim: Coronavirus disease 2019 (COVID-19) reportedly affects many body tissues and organs and is detectable in body fluids, such as saliva and gingival crevicular fluid (GCF). Additionally, COVID-19 can cause an increased GCF volume (GCFV). This study investigated GCFV in patients with a history of COVID-19 infection using periopapers.

Methodology: This study included 50 patients (25 males and 25 females) aged 21–69 years who were considered periodontally healthy and had a history of COVID-19 infection. GCF was collected from the central incisors' buccal sites using paper strips, and GCFV was calculated using a Periotron 8000.

Results: In patients with a history of COVID-19, the mean GCFV for all patients was 0.5226 ± 0.11 µl. The mean was 0.5208 ± 0.1011 µl in men and 0.5244 ± 0.1261 µl in women. No significant difference was found between the two genders regarding GCFV.

Conclusion: Regarding GCFV, no significant difference was found between individuals with a history of COVID-19 infection and those with no history of COVID-19 infection.

Keywords: COVID-19, gingival crevicular fluid (GCF), biomarker, Periotron, periopaper

Introduction

Coronavirus disease 2019 (COVID-19) is a novel viral infection that was first diagnosed in Wuhan, China, and and rapidly spread to all over China and the world. This rapidly spreading virus is more contagious than the Middle East respiratory syndrome coronavirus (MERS) (1). The World Health Organization declared the coronavirus outbreak a pandemic in March 2020 (2). It can induce symptoms such as fever, respiratory distress, cough, and invasive lesions affecting both lungs of the patients. The virus has the ability to propagate to the lower respiratory system, leading to the development of viral pneumonia. Severely affected individuals have dyspnea and respiratory distress syndrome (3). Although 80% of the cases have mild symptoms, severe symptoms have been observed in 20% of cases. In 5% of cases, the disease progressed to a critical stage and resulted in pneumonia or acute respiratory failure requiring mechanical ventilation and intensive care (4). COVID-19 is transmitted predominantly by direct contact with infected people or via droplets (5).

Acute COVID-19 infection alongside associated therapeutic applications can have adverse effects on oral health, namely taste disturbances, vague oral ulcerations, desquamative gingivitis, and opportunistic infections, such as petechiae and candida (4, 6). Human gingival crevicular fluid (GCF) was discovered in the nineteenth century, and Brill and Björn demonstrated its composition and oral defense mechanism in 1959 (7).

Gingival crevicular fluid, an oral bio-fluid that is located near gingival tissues, has been extensively utilized to understand and distinguish between periodontal health and illness (8). The biomarkers found in the gingival crevicular fluid (GCF) can serve as a trusted tool for identifying the subtle alterations observed in disease progression. The GCF contains a combination of substances produced by both the host and bacteria, as well as biomarkers. These biomarkers may be analyzed to determine the presence, severity, and treatment of periodontal disease (8). GCF is a physiological fluid that many researchers classify as an inflammatory exudate, and it is also considered an altered tissue transudation in a healthy state (9). The GCF volume (GCFV) is proportional to the severity of periodontal inflammation, and the release and components of GCF provide significant information about periodontal disease development (10). GCFV can also change in conditions such as smoking (11), bruxism (12), diabetes, and periodontal disease (13).

Periodontal tissue, when inflamed, releases inflammatory factors such as cytokines, bacterial antigens, different cells, metabolites, and other degradation products into the gingival crevicular fluid (GCF) (14). Previous studies have detected COVID-19 in the GCF of patients with a history of COVID-19 (15). Many diseases can be monitored using GCF, with no need for invasive methods (16). GCF is either minimal or absent in healthy gingiva. The GCFV increases with inflammation (17), and its volume can be calculated by collecting GCF via several methods and materials, such as periopapers (18), gingival washing technique, and the use of microcapillary tubules (19) and platinum loops (20) (Fig. 1). Calculating GCFV with periopaper strips is based on estimating the volume change that occurs after the contact of predetermined periopapers with GCF (21). Over the last 10 years, researchers have commonly preferred periopaepr strips because they can easily reach a depth of over 1 mm without causing bleeding in the periodontal pocket (20). The average GCFV was approximately 0.43–1.56 µL in the proximal regions of the molar teeth (22).

This study investigated GCFV in patients with a history of COVID-19 infection using periopapers.

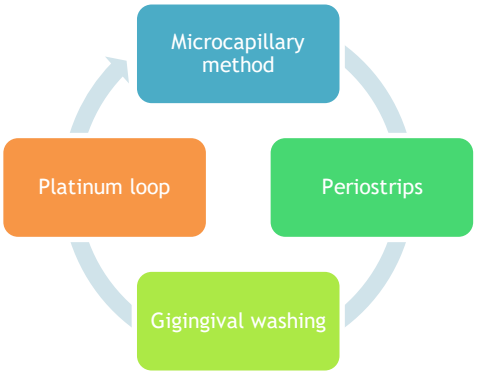

Figure 1. GCF (Gingival crevicular fluid) collection methods

Materials and Methods

This study was conducted in accordance with the ethical rules of the Declaration of Helsinki and was approved by Harran University, Faculty of Dentistry, Local Ethics Committee (Approval No: HRU-21.05.29).

The study had a cohort of 50 individuals, consisting of 25 men and 25 females, with ages ranging from 21 to 69 years. These patients were deemed to be in good periodontal health and had a previous record of being infected with COVID-19.

This study examined GCF in individuals with a history of COVID-19 who were nonsmokers, had no systemic diseases, and were considered periodontally healthy (not diagnosed with periodontitis or gingivitis). GCF collection was performed at the same time of day using the perioaper strip method. GCF samples were only taken from the buccal sites of the right central incisors in each individual to eradicate the possibility of volumetric differences in tooth dimensions (23). Prior to sampling, these sites were isolated with cotton rolls and dried with compressed air. Care was taken to prevent contaminating the periopapers with blood and saliva. Periopapers contaminated with blood and saliva were not included in the study. To ensure standardization, the

periopapers were kept in the tooth groove for 30 seconds and then each periopaper's GCFV was measured using a pre-calibrated Periotron 8000 (Oraflow Inc, New York, USA). GCFV was calculated by converting the obtained value to microliters (µl).

Statistical analysis

Analyses were performed by using SPSS software (IBM SPSS V24, IBM Inc., Armonk, NY, USA).

The descriptive data were expressed as mean, standard deviation (SD), min-max, and median. Normal data distribution was assessed using the Kolmogorov-Smirnov test, and the homogeneity of variance was assessed using Levene's test. Variables with non-normal distributions were compared using the Mann-Whitney U test. A *p*-value of <0.05 was considered significant.

Results

The 50 participants comprised 25 males and 25 females aged 21-69 years. The mean ± standard deviation of the participants' ages was 40.98 ± 15.52 years. The median GCFV of all participants was 0.51 µl (range: 0.23-0.69 µl), while it was 0.51 µl (range: 0.36-0.68 µl) and 0.56 µl (range: 0.23-0.69 µl) for men and women, respectively (Fig. 2).

No significant difference was found between the two genders with regard to GCFV (p = 0.749; Table 1). The mean GCFV was 0.5226 ± 0.11 µl, 0.5208 ± 0.1011 µl, and 0.5244 ± 0.1261 µl for all patients, men, and women with a history of COVID-19, respectively. A negative correlation was found between age and GCFV (*p* = 0.43; Fig. 3).

Table 1. GCFV (Gingival crevicular fluid volume) values of male and female participants

Gender	Median	Min	Max
Female	0.56	0.23	0.69
Male	0.51	0.36	0.68
Total	0.53	0.23	0.69

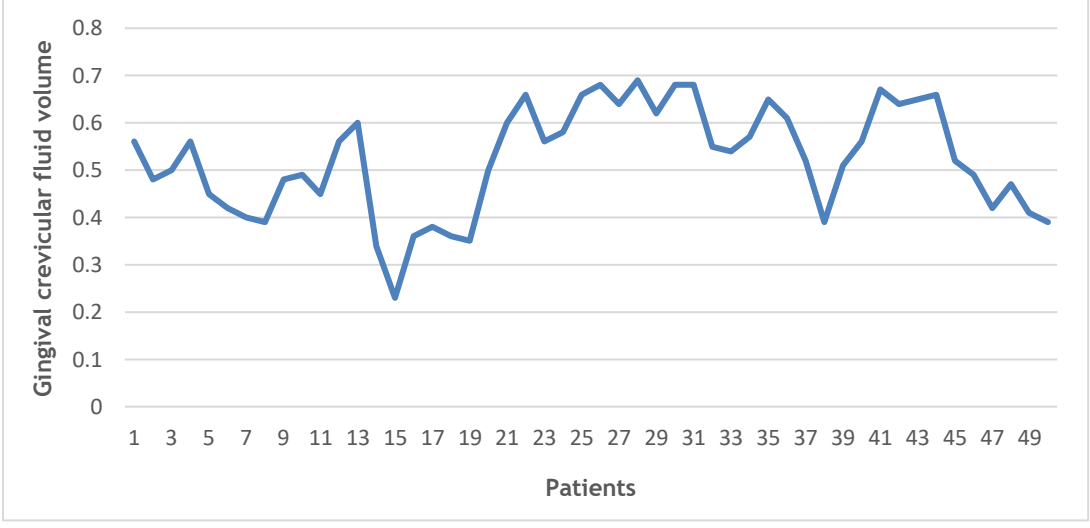

Figure 2. GCFV (Gingival crevicular fluid volume) values of the patients

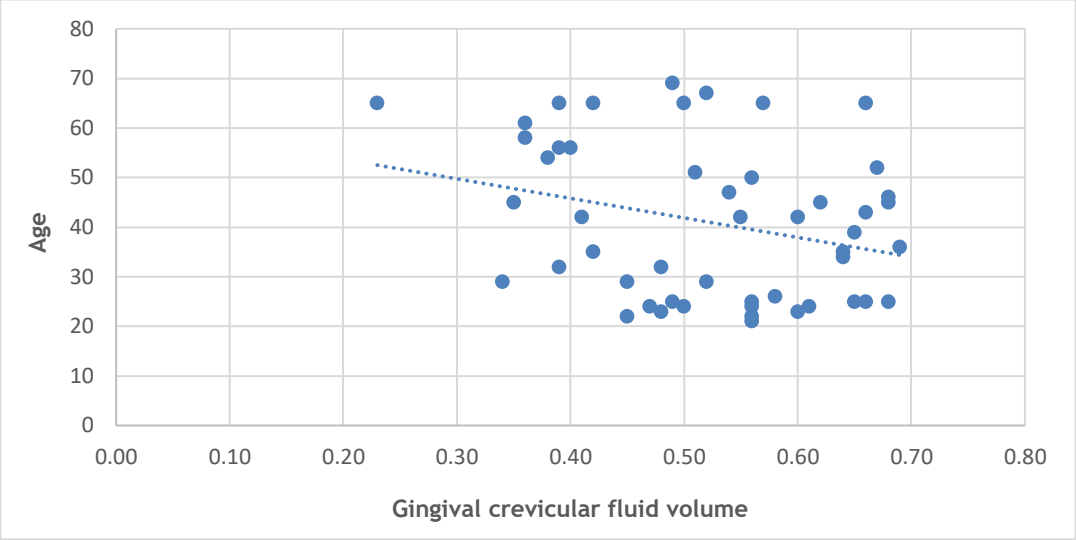

Figure 3. Distribution of GCFV (Gingival crevicular fluid volume) values with regard to age (Negative correlation line).

Discussion

Coronaviruses are a large family of viruses infecting humans and animals. Although these viruses have mostly manifested as mild seasonal flu infections in the past, recent forms of coronaviruses, including severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, MERS-coronavirus (MERS-CoV) in 2012, and SARS-CoV-2 in the last two years, have been shown to cause severe upper respiratory tract infections. SARS-CoV-2, which causes COVID-19, most commonly binds to ACE-2 and TMPRSS2 receptors, causing disease in humans. The respiratory tract is the most common entry route, since the receptors to which the virus binds are mostly located in this tract (24, 25). Additionally, SARS-CoV-2 is considered to be transmitted by droplets that cause the virus to contact and colonize cells in the oral cavity, nose, or eyes (26). Periodontal pockets have specific subgingival environments with a dental root wall that facilitates the formation of complex subgingival biofilms and a mucosal wall formed by an ulcerated epithelium with exposed connective tissue. It has been hypothesized that periodontal pockets could be a reservoir for the SARS-CoV-2 virus and that the virus could replicate in periodontal pockets to mix with saliva or migrate systemically (27).

Researchers have been searching for a non-invasive way to collect and measure the amount of gingival fluid in order to determine the severity and predict the incidence of periodontal disease, due to the association between gingival fluid volume and the stage of periodontitis (28, 29). Periodontal health is known to reflect systemic health. Based on this fact, GCF has been utilized in several studies as an indicator of the serum level of immune markers to measure the systemic status of individuals. Additionally, GCF samples have been used to reliably determine viral loads when examining periodontal conditions (30). In the present study, we analyzed GCFV by considering that SARS-CoV-2 could be an affecting factor.

Accumulating evidence suggests that GCFV can be affected by numerous factors, including circadian rhythm, periodontal surgical treatment, smoking, orthodontic treatment, X-rays, and mechanical stimuli, such as hard tooth brushing, gingival massage, and consumption of hard foods (31, 32). Additionally, Urbaniak et al. showed that hormonal changes in the menstrual cycle can cause an increase in GCFV (33). Bergman et al. reported that GCFV is subject to circadian rhythm that falls and rises at different times of the day (34), while Günday et al. reported that GCFV did not change with circadian rhythm (23). In our study, we paid the utmost attention to standardize the factors that have been shown to have the potential to affect GCFV and that could be controlled in terms of sampling methodology (e.g., circadian rhythm, saliva or blood contamination, severity of mechanical irritation, smoking status, hard brushing habit, and hard food diet).

To date, numerous methods have been utilized for the determination of GCFV (35, 36). Of these, the paper strip method has become the method of choice and has been shown to produce relatively more robust results compared to other approaches (32, 33, 35). Therefore, in the present study, we used the paper strip method for collecting GCF due to its numerous advantages, such as high patient satisfaction, easy application, and short application time.

Many studies have shown that age and gender have no effect on GCF flow rate, volume, and content (37–39). In our study, although gender had no effect on GCFV, unlike in other studies, a negative correlation was observed between age and GCFV.

Previous studies have reported a wide range of GCFV values (40–42). In one of these studies, GCFV was found to range between 0.24 µL and 0.43 µL in the presence of healthy gingiva in anterior teeth (42).

Griffiths et al. reported that GCFV in healthy sites ranged between 0.02 µl and 0.71 µl (40). Lamster et al. found that GCFV ranged from 0.18 µl to 0.46 µl in cases of gingivitis and between 0.41 µl and 0.79 µl in cases of periodontitis (43). Mokeem et al. reported mean GCFV in smokers and nonsmokers as 0.25 ± 0.04 µl and 0.31 ± 0.05 µl, respectively. The authors emphasized that smokers had lower GCFV compared to nonsmokers (35).

Nijakowski et al. evaluated the effect of bruxism on GCFV and reported that the GCFV ranged between 0.12 µL and 69 µL in anterior teeth and between 0.24 µL and 0.93 µL in posterior teeth. The authors also noted that bruxism leads to increased GCFV (12).

Marcaccini et al. explored the effect of periodontal treatment on variables such as GCFV, MMP8, and MMP9 and determined periodontal GCFV to be 0.43 ± 0.35 µL in gingivitis patients and 0.7 ± 0.41 µL in periodontitis patients before treatment (44). In healthy human gingiva, GCFV ranges between 0.5 µL and 2.5 µL during the day (31, 45, 46). In contrast, a rat study that evaluated the effect of panoramic radiography on GCFV reported the mean GCFV as 0.288 µL, 0.294 µL, and 0.372 µL in periodontitis rats exposed to X-rays once, twice, and three times, respectively (47). In our study, the mean GCFV was 0.5226 ± 0.11 µL in patients with healthy gingiva and a history of COVID-19 infection within the previous month. A comparison of this volume with that reported in previous studies showed similar GCFV in patients with healthy gingiva and those with a history of COVID-19 infection.

Conclusion

In conclusion, a review of the literature revealed that the GCFV in individuals with a history of COVID-19 infection was similar to that of healthy individuals with no history of COVID-19 infection. Additionally, the findings indicated that the mean GCFV was similar in men and women and that a negative correlation was noted between GCFV and age. Due to the small sample size of our study, these findings should be supported by further studies with larger sample sizes.

Disclosures

Ethical Approval: Ethics committee approval was received for this study from the Harran University, Faculty of Dentistry, Local Ethics Committee, in accordance the World Medical Association Declaration of Helsinki, with the approval number: HRU-21.05.29.

Peer-review: Externally peer-reviewed.

Author Contributions: Conception – D.D.Ü.; Design – D.D.Ü., B.S.İ.; Supervision – B.S.İ.; Materials – D.D.Ü.; Data Collection and/or Processing – B.S.İ.; Analysis and/or Interpretation – D.D.Ü.; Literature Review – D.D.Ü. B.S.İ.; Writer – D.D.Ü.; Critical Review –B.S.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Funding: The authors declared that this study has received no financial support.

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