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ORIGINAL RESEARCH

Comparison of Salivary Secretion, pH, and Buffer Capacity Between COVID-19 Vaccinated and Unvaccinated Child Patients Visiting Dental Clinics of University Hospitals in Riyadh City, Saudi Arabia

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Objective: This study aimed to assess and compare the salivary secretion, pH, and buffer capacity between COVID-19 vaccinated and unvaccinated child patients visiting the clinics of private university dental hospitals in Riyadh, Saudi Arabia.
Methods: This is the first comparative assessment of salivary parameters between unvaccinated and COVID-19-vaccinated child patients. The study sample comprised COVID-19 unvaccinated (n = 66) and vaccinated (n = 66) pediatric dental patients aged 4–12 years seeking dental care in clinics of private university hospitals. Paraffin-stimulated saliva was collected from unvaccinated and vaccinated study participants, and the amount of saliva secreted per minute was noted. Salivary pH and buffering capacity (by 5 mmol Hydrochloric acid titration) were measured using a benchtop digital pH meter. The data obtained were compared between unvaccinated and vaccinated participants using an independent *t*-test.
Results: The results showed a significantly higher salivary secretion rate in unvaccinated than vaccinated study participants (0.83 ± 0.24 mL/min vs 0.67 ± 0.24 mL/min, $p = 0.001$). Similarly, unvaccinated subjects compared to vaccinated subjects exhibited a significantly higher pH (7.33 ± 0.39 vs 7.04 ± 0.46, $p < 0.001$) and buffering capacity (6.31 ± 1.55 vs 5.40 ± 1.22, $p < 0.001$). Moreover, unvaccinated females demonstrated a significantly higher salivary secretion (0.87 ± 0.23 vs 0.71 ± 0.25, $t = 2.627$, $p = 0.011$) and buffering capacity 6.19 ± 1.52 vs 5.34 ± 1.25, $t = 2.404$, $p = 0.019$) than vaccinated females. Similarly, unvaccinated male exhibited significantly higher salivary secretion (0.80 ± 0.25 vs 0.64 ± 0.23, $t = 2.670$, $p = 0.009$), salivary pH (7.39 ± 0.45 vs 6.94 ± 0.41, t=4.309, p<0.001) and buffering capacity (6.42 ± 1.60 vs 5.45 ± 1.21, $t = 2.875$, $p = 0.005$) than the vaccinated male subjects.
Conclusion: The vaccinated subjects showed a significantly lower mean salivary secretion, pH, and buffering capacity than unvaccinated participants. Hence, COVID-19 vaccination is likely to affect salivary parameters among pediatric patients.
Keywords: COVID-19, vaccine, salivary secretion, pH, buffer, pediatric, patients

Introduction

On March 11, 2020, the World Health Organization (WHO) officially declared the ongoing epidemic of the new coronavirus disease (COVID-19) as a worldwide pandemic. A cluster of pneumonia cases in the Chinese city of Wuhan, Hubei province, was attributed to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Individuals experiencing minor respiratory symptoms were strongly advised to self-isolation and social distancing to mitigate the risk of spreading the disease.[1]

In the early phases of the COVID-19 pandemic, the number of confirmed cases among children was low, and it was believed that SARS-CoV-2 rarely affected the children.[2] The reasons behind variations in epidemiology, clinical

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manifestations, and prognoses of COVID-19 between children and adults remained unclear.[2] Subsequent studies consistently demonstrated that children and adolescents are susceptible to SARS-CoV-2 infection. However, many children were either asymptomatic or pre-symptomatic, so the incidence of infection was under-reported because of limited testing among children.[3] It was noted that the children infected with COVID-19 often experience fever, cough, nausea, and vomiting, while older children and adolescents may experience chills, rigors, malaise, headaches, and myalgia.[4] Few pediatric patients had gastrointestinal symptoms. Most infected children reported previous contact with an infected individual.[5] The most frequent laboratory abnormalities observed were leukopenia, lymphopenia, thrombocytopenia, increased lactate dehydrogenase, and raised alanine aminotransferase. Radiographic abnormalities were seen in almost all laboratory-confirmed cases of SARS CoV-2 in children. The main radiographic finding was the presence of ground-glass opacities and/or regions of consolidation that were unifocal, lobar, or multifocal.[5,6]

In general, the incidence and mortality rates of COVID-19 disease among children and adolescents were comparatively lower when compared to the adult population. The age-specific data of the World Health Organization (WHO) observed that the children under age of 5 accounted for 1.8% (1,695,265) of the total reported cases of COVID-19 worldwide. Additionally, this age group represented 0.1% (1721) of the total reported deaths globally. Children and adolescents between the ages of 5 and 14 accounted for 6.3% (6,020,084) cases worldwide with 0.1% (1245) fatalities. In contrast, older adolescents and young adults aged 15 to 24 represented 14.5% (13,647,211) of global cases, with higher mortality rate of 0.4% (6436).[7]

Study conducted in Saudi Arabia indicated less severe symptoms and a lower likelihood of hospital admission and life-threatening complications among children infected with SARS-COV-2.[5] Asymptomatic children infected with SARS-CoV-2 were less likely to transmit the virus than symptomatic.[8] In contrast, few studies reported that many SARS-CoV-2-infected children who are asymptomatic or presymptomatic may continue to shed the virus for 2–3 weeks. These results are important for public health initiatives to reduce and restrict spread, especially when areas of affected communities are recovering from the infection.[9,10] In light of the global pandemic and the continuous emergence of SARS-CoV-2 variants, it was crucial to prioritize and expedite vaccination efforts while also striving to increase vaccination coverage.[11]

The safety and effectiveness of SARS-CoV-2 vaccines are highly encouraging, in consistently reducing mortality, severe illness, symptomatic cases, and infections caused by SARS-CoV-2 globally. SARS-COV-2 vaccination was the optimal solution for effectively mitigating and eliminating the pandemic.[11] Although uncommon, some children may have severe illness after infection with the COVID-19 virus. The administration of a COVID-19 vaccine has the potential to protect children against contracting COVID-19. Additionally, it may minimize the risk of children experiencing severe illness or requiring hospitalization.

The Centers for Disease Control and Prevention (CDC) recommended that children older than six months get a COVID-19 immunization, adding that children who have been infected with COVID-19 in the past would receive increased protection from the vaccine. The recommendation was provided after the Food and Drug Administration approved two long-awaited COVID-19 vaccines for children under five. The two vaccines were the Pfizer-BioNTech COVID-19 vaccine for ages six months to four years and Moderna COVID-19 for ages six months to seventeen. The Pfizer-BioNTech vaccine is provided in a primary series of three doses and the Moderna vaccine in two doses (with a third significant dose for immunocompromised children).[12]

In June 2021, the Saudi Ministry of Health (MoH) extended its COVID-19 immunization recommendations to include children older than 12 years for the Pfizer-BioNTech and Moderna vaccines.[13] This was announced after safety and effectiveness of vaccines in children aged 12 to 18 years[14,15] was reported. By September 2021, over 90% of school-aged children aged 12 to 18 were vaccinated against COVID-19.[16] Later, the Pfizer-BioNTech vaccine was found to be safe and effective in children 5–11 years old.[17] On November 3, 2021, the Saudi Food and Drug Authority (SFDA) provided emergency vaccine approval for use in this population.[18] However, the Saudi Ministry of Health did not approve COVID-19 vaccination for children 5–11 years old until February 2022, hence the immunization was not required against COVID-19 for this age group.

The SARS-CoV-2 virus has shown a specific affinity to epithelial host cells in the salivary gland by binding to ACE-2 receptors.[19] Numerous clinical presentations linked to coronavirus disease (COVID-19) have been documented in the oral cavity, encompassing taste impairment, oral mucosal abnormalities, and disturbances in salivary gland function.[20] The detection of SARS-CoV-2 in saliva and presence of xerostomia suggests the potential infiltration of the virus into the salivary gland.[21]

The extracted data from 18 cross-sectional studies conducted in Saudi Arabia revealed a very high prevalence of dental caries among children. The prevalence of caries among children aged 5–7 years was determined to be 84%. Similarly, a 72% prevalence of caries was seen among children aged 12–15 years.[22] Salivary factors could play an important role in caries process. The flow of saliva and its buffering capacity are vital factors that play a substantial role in maintaining oral health.[23] The salivary buffer systems play a critical role in maintaining the appropriate acid-base balance relatively stable pH level.[24]

Salivary buffers can counteract the acidic pH levels found in dental plaque, thereby facilitating oral clearance. Consequently, this process helps prevent the demineralization of tooth enamel. Saliva, by its buffering capacity, is pivotal in preserving dental integrity. It achieves this by exerting control over the demineralization process and facilitating the ongoing promotion of enamel remineralization.[25] Multiple research studies have established a significant association between saliva's buffering capacity and dental caries' activity. This correlation has been utilized to effectively anticipate and identify the risk of dental caries in medically vulnerable individuals.[26,27]

Occasional documentation of oral adverse effects after COVID-19 vaccinations have been observed requiring further investigation into the vaccine-elicited response on salivary parameters.[28] The negative impacts of COVID-19 vaccine on the salivary glands may contribute to an increased susceptibility to dental caries among children, leading to a rise in both the prevalence and severity of the condition. Hence, further investigation is warranted to elucidate the ambiguous effects of COVID-19 vaccination on salivary secretion, pH levels, and buffering capacity in pediatric populations.

The main objective of this study was to assess the differences between salivary quantity, pH and salivary buffer capacity amongst COVID-19 vaccinated and unvaccinated child patients visiting the clinics of the University Dental Hospital in Riyadh, Saudi Arabia.

The null hypothesis tested in this study states that there would be no significant differences in salivary quantity, pH, and buffer capacity between COVID-19 vaccinated and unvaccinated child patients.

Materials and Method

Ethical Approval

The study proposal was submitted to the research and innovation center of Riyadh Elm University (REU) and the approval for the study (FPGRP/2022/704/810/805) was obtained from REU ethics committee on 27-Oct-2022. The researcher fully explained the child's guardian/caretakers about risks and benefits of participation in the study. The personnel identifier information of study participants was coded and the data on salivary parameters were recorded anonymously, and data confidentiality was assured. The participant's guardian/caretakers were informed about the use of data on research and publication purposes only. All the research information was provided to the participants. Moreover, participants were free to withdraw from study at any time. The contact details of the investigator were provided to ask any queries related to the research. The guardian/caretakers after understanding the content in their local Arabic language signed the informed consent on paper and a copy which was given to them. The child patient's assent was also obtained for the study participation.

Study Design

It was a comparative study of salivary parameters (salivary secretion, pH, and buffer capacity) between COVID-19 vaccinated and unvaccinated pediatric dental patients.

Sample Size Calculation

The sample size was determined using G*Power (version 3.1.9.7), a software tool specifically designed to compute sample size and statistical power. A sample of 132 child dental patients (COVID-19 vaccinated = 66 and unvaccinated = 66) was calculated based on medium effect size d = 0.5, α error probability = 0.05, power (1-β error probability) = 0.81. This sample size was justified based on available time, resources and number of child patients seeking dental care at university dental hospitals.

A convenience sampling technique was employed to select the study participants based on COVID-19 vaccination status (vaccinated versus unvaccinated) and without any randomization process.

Study Subjects and Selection

Pediatric dental patients attending clinics of Riyadh Elm University hospitals were considered in this study based on the following inclusion and exclusion criteria.

Inclusion Criteria

Male and female dental patients aged 4–12 years who were free from any underlying medical conditions.

Patients were not taking any medications.

Patients with COVID-19 vaccination status recorded in the Tawakkalna Application.

The willingness of the patient's parents or guardians to participate in the research.

Exclusion Criteria

Aged below 4 years and above 12 years.

Patients with cancers or other severe conditions that impair overall health.

Individuals have dryness of the mouth due to radiation or autoimmune disorders.

Patients affected with Sjögren's syndrome, sialolithiasis, and sialadenitis.

Individuals undergoing treatment that impacts the properties of their saliva, such as administering antibiotics, corticosteroids, anticonvulsants, antiparkinsonian agents, antipsychotics, antidepressants, and Proton Pump Inhibitor therapy, among others.

Highly uncooperative patients and those not willing to agree to participate in the study.

Parents refused to participate in the study.

Examiner Training

Single examiner (HAE) was trained to collect pediatric patients' salivary parameters. The salivary secretion rate per minute, salivary pH and buffering capacity were measured under the supervision of biochemistry professor.

Determining the COVID-19 Vaccine Status

The Tawakkalna application is a versatile and multifunctional mobile application that was launched in Saudi Arabia in April 2020 to regulate people's movement during pandemic. The Ministry of Health (MOH) introduced the Immunity Passport service in January 2021 as a new feature of the application. The application documented the user's COVID-19 vaccine doses, including the brand name and date of administration. Users can conveniently obtain the vaccination certificate through the application by utilizing their national ID or residence permit number for authentication purposes. The Tawakkalna application can be freely downloaded from the playstores on any smart phone. This application was easy to use and provided accurate and reliable information on the vaccination status of the participants. Vaccination status of all the family members can be linked with one mobile number under family head. Hence, the child's parents/caregivers were requested to provide their COVID-19 vaccine status based on Tawakkalna records at the time of examination.

Collection of Saliva

Paraffin-stimulated saliva was collected from vaccinated and unvaccinated child patients. Sampling was carried out in the morning to decrease circadian variations' influence on the salivary flow rate. The study subjects refrained from eating, drinking, or chewing gum for nearly 90 min before sampling. A trained single investigator performed all saliva sampling. Before sampling, children were left to relax for 5 min sitting upright, with their heads bent slightly forward. In order to obtain saliva samples, the participants were instructed to place a 7.01 g piece of paraffin in their oral cavity for 30 seconds to soften it. Swallowing the accumulated saliva marked the beginning of the timing process. The participants were instructed to orally process the paraffin using their normal masticatory process and to periodically expel the resultant saliva into a measuring vessel at one-minute intervals. Following 5 minutes, the volume that was amassed underwent measurement, and subsequently, the rate of saliva flow was calculated in milliliters per minute. The salivary samples were promptly transported to the laboratory for analysis on the same day. The sample analysis was carried out in the biochemistry laboratory located at Riyadh Elm University to measure the pH and buffering capacity.

Measurement of Salivary pH

The pH meter device comprises a pH electrode that utilizes a flow combination design. It is equipped with a free-flow junction, rendering it suitable for application with contaminated or viscous samples. The pH range of this electrode spans from 0 to 14, and it is furnished with a refillable internal reference composed of silver/silver chloride (Ag/AgCl). Additionally, the electrode is equipped with an external reference of 4M KCI, extending its lifespan. The device features an epoxy body that extends coverage beyond the sensing bulb, enhancing its durability.

Additionally, it is equipped with a waterproof Bayonet Neill-Concelman (BNC) connection, which is accompanied by a 1 m (39”) cable. The electrode is equipped with a small orifice to facilitate the replenishment of the KCl fill solution, thereby extending the longevity of the electrode. The electrode’s free-flow junction enables its applicability in testing dirty and viscous samples. The junction may be effectively cleansed by depressing the cap in the interim period between measurements, thereby facilitating the unobstructed flow of the filling solution through the junction and the consequent elimination of any impurities. The physical attributes of the body include a length of 120 mm (4.72 inches) and a diameter of 12 mm (0.47 inches), while the cap has a diameter of 16 mm.

Additionally, the device is equipped with a cable measuring 39 inches (1 meter) in length. The electrode was submersed in the specimen within an enclosed vessel, and the digital measurement was permitted to stabilize for a few seconds. The final stable reading was taken as the salivary pH value.

Measurement of Salivary Buffering Capacity

The buffering capacity of the saliva was measured by quantitative test using a pH meter. This method involves the addition of 0.5 mL of saliva to 1.5 mL of 5mmol/L HCl acid. The mixture was vigorously shaken in Sonicator (Branson Sonicator) to eliminate the carbon dioxide from the sample. The sample was permitted to stand for 10 minutes, following which the final pH value was determined using the same pH meter. The pH meter’s consistency was monitored regularly using pH 4.1, 7, and 10.01 standard buffers. The buffering capacity of the sample was calculated using the following formula.

Buffer capacity = pH after the addition of 1.5 mL of HCl/pH difference before and after HCl.

The categorization of the salivary buffering capacity value at 1.5 mL of 5 μmol/l titrations of HCl was based on the established criteria outlined by Moritsuka et al and classified into three distinct categories: low buffering capacity ($pH < 4.5$), medium buffering capacity (pH 4.5–5.5), and high buffering capacity ($pH > 5.5$).[29]

Statistical Analysis

Statistical analysis was performed using the statistical analysis software IBM-SPSS 25 (Armonk. NY: USA). Descriptive statistics of frequency distribution and mean and standard deviation were calculated. The normality of the data was checked based on Shapiro–Wilk’s test and Kolmogorov–Smirnov test. Data was found to be normally distributed ($p>0.05$) salivary pH and buffer capacity. Therefore, an independent *t*-test was applied to compare the mean salivary pH and buffer between unvaccinated and vaccinated subjects. The chi-square test was applied to compare the vaccination status across different buffering categories (low, medium, and high). The significance level of $p<0.05$ was considered for all the statistical tests.

Results

A total of 66 (50%) unvaccinated and 66 (50%) vaccinated pediatric dental patients participated in this study. Gender distribution showed that 70 (53%) participants were males and 62 (47%) were females. Nearly 113 (85.6%) of participants were selected from the Munasiyah campus, and 19 (14.4%) were recruited from the Namuthajiya campus. Most participants were Saudi nationals, 124 (93.9%), and the rest were non-Saudi nationals, 8 (6.1%). The characteristics of the study participants are shown in Table 1. The mean age of unvaccinated patients was 7.91 ± 1.94 years, while vaccinated patients had a mean age of 10.09 ± 1.72 years.

The salivary secretion was found to be significantly higher in unvaccinated (0.83 ± 0.24 mL/min) subjects than in vaccinated (0.67 ± 0.24 mL/min) subjects ($p = 0.001$). A salivary pH and buffering capacity were compared between unvaccinated and vaccinated subjects using an independent sample *t*-test. The unvaccinated (7.33 ± 0.39) subjects showed a significantly higher mean salivary pH value than the vaccinated study participants (7.04 ± 0.46) ($p < 0.001$). Similarly, unvaccinated subjects (6.31 ± 1.55) demonstrated a higher buffering capacity than the vaccinated study subjects (5.40 ± 1.22), and the difference was statistically significant ($p < 0.001$) (Table 2).

The salivary secretion, pH, and buffer comparison between unvaccinated and vaccinated males and females is displayed in (Table 3). The unvaccinated female (n = 31) participants showed a significantly higher salivary secretion (0.87 ± 0.23 vs 0.71 ± 0.25, $t = 2.627$, $p = 0.011$) and buffering capacity (6.19 ± 1.52 vs 5.34 ± 1.25, $t = 2.404$, $p = 0.019$) than the vaccinated female (n = 31) subjects. However, pH did not differ significantly between vaccinated and unvaccinated female participants (7.28 ± 0.29 vs 7.14 ± 0.49, $t = 1.305$, $p = 0.198$). Similarly, the unvaccinated male (n = 35) children showed a significantly higher salivary secretion (0.80 ± 0.25 vs 0.64 ± 0.23, $t = 2.670$, $p = 0.009$), salivary pH (7.39 ± 0.45 vs 6.94 ± 0.41, $t = 4.309$, $p < 0.001$) and buffering capacity (6.42 ± 1.60 vs 5.45 ± 1.21, $t = 2.875$, $p = 0.005$) than the vaccinated male (n = 35) subjects.

The buffering capacity of the saliva in unvaccinated and vaccinated study participants presented in (Table 4). The distribution of unvaccinated and vaccinated subjects in low (33.3% vs 66.7%), medium (28.1% vs 71.9%), and high (64.5% vs 35.5%) buffer categories showed a statistically significant difference (df = 2, chi-square value = 15.160, $p = 0.001$). Most of the unvaccinated

Table 1 Characteristics of the COVID-19 Vaccinated and Unvaccinated Children

Variables		**Unvaccinated (n = 66)**		**Vaccinated (n = 66)**		**Total (n=132)**	
		n	**%**	**n**	**%**	**n**	**%**
Campus	Namuthajiya	13	68.4%	6	31.6%	19	14.4%
	Munasiyah	53	46.9%	60	53.1%	113	85.6%
	Total	66	50.0%	66	50.0%	132	100%
Gender	Female	31	50.0%	31	50.0%	62	47%
	Male	35	50.0%	35	50.0%	70	53%
	Total	66	50.0%	66	50.0%	132	100%
Nationality	Saudi	63	50.8%	61	49.2%	124	93.9%
	Non-Saudi	3	37.5%	5	62.5%	8	6.1%
	Total	66	50.0%	66	50.0%	132	100%

Table 2 Descriptive Statistics for Salivary Parameters of Unvaccinated and Vaccinated Subjects

Variables	**Unvaccinated (n = 66)**	**Vaccinated (n = 66)**	***t***	***p***
	Mean± SD	**Mean± SD**		
Saliva Secretion (mL/min)	0.83±0.24	0.67±0.24	3.735	<0.001
Saliva pH	7.33±0.39	7.04±0.46	4.049	<0.001
Buffer capacity at 5 mmoL HCl titration	6.31±1.55	5.40±1.22	3.764	<0.001

Abbreviations: HCl, hydrochloric acid; mL/min, millilitre/minute; SD, standard deviation.

Table 3 Salivary Secretion, pH, and Buffer Between Vaccinated and Unvaccinated Gender

Variables	Females (N = 62)						Male (N=70)					
	Unvaccinated (n = 31)		Vaccinated (n = 31)		*t*	*p*	Unvaccinated (n=35)		Vaccinated (n=35)		*t*	*p*
	Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Salivary secretion	0.87	0.23	0.71	0.25	2.627	0.011	0.80	0.25	0.64	0.23	2.670	0.009
Salivary pH	7.28	0.29	7.14	0.49	1.305	0.198	7.39	0.45	6.94	0.41	4.309	<0.001
Buffering capacity at 5 mmol HCl titration	6.19	1.52	5.34	1.25	2.404	0.019	6.42	1.60	5.45	1.21	2.875	0.005

Abbreviations: mmol, millimoles; HCl, hydrochloric acid; SD, standard deviation; mL/min, millilitre/minute.

Table 4 Buffer Capacity of Saliva in Unvaccinated and Vaccinated Subjects

Buffer	Unvaccinated		Vaccinated		Total	df	Chi-Square	*p*
	n	%	n	%	N			
Low	8	33.3%	16	66.7%	24	2	15.160	0.001
Medium	9	28.1%	23	71.9%	32			
High	49	64.5%	27	35.5%	76			
Total	66	100%	66	100%	132			

Abbreviation: df, degrees of freedom.

children had a higher buffering capacity of the saliva than the vaccinated children. In contrast, most vaccinated children had a low buffering capacity of the saliva.

Based on the current study findings it can be speculated that the COVID-19 vaccination could affect the salivary secretion, buffering capacity and pH among children. The gender differences were obvious with vaccinated males and females demonstrating lowered salivary parameters.

Discussion

This was the first study that assessed the salivary parameters (secretion rate, pH, and buffer) between COVID-19 vaccinated and unvaccinated child patients. The results showed that the salivary secretion, pH, and buffering capacity were significantly lower among vaccinated than the unvaccinated child patients. Hence, the null hypothesis of no differences in salivary parameters between vaccinated and unvaccinated child patients has been rejected.

The oral tissues perform various functions, including mastication, deglutition, taste sensation, speech, and initial digestion of carbohydrates. These functions are reliant on the secretion of saliva.[30] The collection of the human whole saliva can be conveniently achieved by expectorating it into a calibrated container. Many human population based studies have documented unstimulated or stimulated saliva flow rates.[31,32] A striking positive correlation exists between the salivary flow rates in unstimulated and stimulated conditions.[33] The stimulated salivary flow approach has been identified as a suitable and effective technique for measuring salivary flow in patients with suspected dry mouths. This technique is also helpful in qualitatively examining the obtained saliva.[34] Hence, in this investigation stimulated saliva of the COVID-19 vaccinated and unvaccinated pediatric patients was considered to investigate salivary secretion, pH and buffering capacity.

The present investigation ascertained the vaccination status of child patients by means of inquiring with their respective guardians or caretakers regarding the administration of any COVID-19 immunization. Furthermore, the Tawakkalna application was utilized to confirm the vaccination status of children by cross-referencing all COVID-19 data.

Generally, the stimulated salivary flow secretion rate in children has been found to fluctuate between 0.1 and 6 mL/min, exhibiting considerable inter- and intra-individual variability.[31,35,36] As the children grow their salivary flow tends to increase, and male children tend to produce more saliva than females.[37] This study's stimulated salivary secretion rate is similar to the previous reports.[31,38] However, a relatively higher salivary secretion rate was observed in females than in males. Despite the higher mean age of vaccinated children, the unvaccinated participants showed an increased salivary secretion rate. In addition, unvaccinated females and males demonstrated a significantly higher salivary secretion than vaccinated females and males. It can be speculative that the reduced salivary secretion and resulting dry mouth could be adverse oral effects of COVID-19 vaccination. According to previous studies, this condition was more common among older individuals and did not exhibit any preference for a specific vaccine brand. Moreover, active surveillance of self-reported COVID-19 vaccine side effects has yielded 0.4% to 2.7% prevalence rates of xerostomia.[39,40]

In this study, COVID-19 vaccinated patients had a lower salivary secretion rate than the unvaccinated children suggesting a potential association between humoral immune response elicited by COVID-19 vaccination, as evidenced by reduced salivary secretions that remain uncertain.[41,42] This finding is supported by a previous study in which the salivary quantity ranged from 2.00 to 4.50 mL, with a mean of 3.17 ± 0.61.[43] However, xerostomia subsequent to COVID-19 vaccination may pose a potential threat for high prevalence and severity of dental caries leading to dental pain, eating difficulties, speech and appearance, thereby resulting in poor quality of life for the children.

The production rate significantly influences the pH of saliva. During nighttime hours, the rate of salivation is comparatively lower than diurnal hours, resulting in a pH range of approximately 6.2–6.5. The pH level of saliva has the potential to elevate to approximately 8.0 as a result of heightened bicarbonate ion concentration.[44] The concentration of hydrogen ions significantly influences the physicochemical processes occurring in the oral cavity. The pH of saliva is a variable parameter that experiences notable fluctuations due to salivary secretion rate, daily circadian rhythm, dietary intake, systemic pathologies, and the autonomic nervous system.[45] In this study, the pH of saliva was measured using a pH meter, a widely accepted laboratory technique for immediate measurement of collected saliva. The composition of saliva is so intricate that it is exceedingly challenging to reproduce it using individual constituents.

Typically, the pH range of saliva is maintained within 6.7 to 7.4 in a state of good health.[30] Repeated consumption of sugar-rich dietary components and acidic fluids, such as fruit juices and carbonated beverages, might occasionally lower the pH levels of saliva. Salivary detection of certain hormones, such as cortisol, aldosterone, testosterone, estradiol, or insulin, is strongly associated with their levels in the bloodstream. Nevertheless, fluctuations in these hormone levels during physiological changes may impact the pH of saliva. In this study, salivary pH of 7.33 ± 0.39 and 7.04 ± 0.46 was observed among unvaccinated and vaccinated participants. These pH values were within the normal ranges and well above the critical pH (5.5). The significant difference observed in the pH may be attributed to the elevated immunologic factors in saliva (IgA, IgG, and IgM) subsequent to COVID-19 immunization.

Unvaccinated male participants exhibited significantly higher pH levels than their vaccinated counterparts, while no such significant difference in salivary pH levels between vaccinated and unvaccinated females was observed. Therefore, it can be speculative that the COVID-19 vaccine is more likely to cause variation in the salivary pH of male children than females. The pH level of saliva is influenced by several variables, including hormonal, immunological, microbiological, and diet-related aspects.

Saliva provides both static and dynamic protective effects. The static effects offer continuous protection, while the dynamic effects provide protection during a challenge. The dynamic effects of saliva, namely salivary buffering capacity, play a crucial role in preventing demineralization of tooth structure.[30] The hydrogen carbonate ions (HCO3) are crucial in preserving saliva's homeostasis, chemical stability, and buffer capacity. The concentration level positively correlates with the saliva volume, reaching its maximum point at 40–60 mmol/l. This concentration level is notably higher than the concentration of the same anion in the blood plasma, as reported in a previous study.[46] A rise in the HCO3 concentration is concomitant with an elevation in salivary pH. The observed value ranges from 5.6 during basal secretion to 7.8 during maximal secretion. The concentration of H+ ions remains relatively constant in saliva that is not stimulated.

Moreover, the pH stability is maintained by buffering agents such as bicarbonates, phosphates, proteins, free amino acids, ammonia, and urea.[47] Stimulated salivary flow is positively correlated with the buffering capacity of the saliva among children.[48] This study found a significant difference in the salivary buffering capacity of the unvaccinated and vaccinated children. Vaccinated study participants showed a significantly lower buffering capacity than unvaccinated subjects. Since an association exists between the buffering capacity of saliva and caries activity, it is possible to predict and detect the risk of dental caries and update dental treatment protocols leading to an improvement in the oral health status of COVID-19 vaccinated children.

The gender specific differences were reported in the salivary parameters. It has been shown that the females demonstrated lower levels of salivary secretion rate, pH and buffer capacity than males. The observed variations in salivary parameters might potentially be attributed to sexual dimorphism in salivary gland structure and distinct gene-expression patterns. Other factors that could influence salivary parameters in children were the age, body mass index and protein calorie malnutrition.[47,49] However, in this study, salivary parameters were found to be lower in vaccinated male and female participants compared to the unvaccinated children despite higher age of the vaccinated study participants and considering salivary circadian rhythm. This gender difference represents a novel finding that may be speculative of the fact that the COVID-19 vaccine may affect salivary parameters in children. More studies are needed to confirm the current study findings.

Study Implications

The primary benefit of the current investigation is its novelty in presenting the salivary parameters of vaccinated and unvaccinated child patients for the first time after COVID-19 vaccination commenced among eligible children. The epidemiological studies in Saudi Arabia have revealed a significant prevalence and severity of dental caries among the pediatric population. The findings of this study may potentially have significant implications for the oral health of children, as the significant decrease in salivary secretion rate, pH and buffering capacity may further escalate the prevalence and severity of dental caries in this population. Consequently, this may place an additional burden on the provision of dental care services on long term.

Limitations

This study has not considered other factors affecting salivary secretions, such as race, geographical area, socioeconomic conditions, nutritional status, body mass index, and salivary gland size. Secondly, the time elapsed between vaccine administration and data collection has not been recorded. Oral health variables and salivary parameters in unvaccinated and vaccinated children have not been correlated in this study. Caution should be taken while generalizing the study's findings since the study participants were child patients attending dental clinics from a single university dental school. Despite conducting a thorough review of existing literature, we could not find any study that specifically investigated the impact of COVID-19 vaccination on salivary parameters (such as salivary secretion, pH, and buffer) in children. Therefore, we did not come across any study that may directly or indirectly support or contrast our findings.

Given the limitations of the present study and the need to determine the long-term effects of COVID-19 vaccination on salivary parameters in children, it is recommended to conduct a multicenter randomized control trial in order to obtain generalizable findings. Additionally, these studies should take into consideration the oral health status, behavioural and dietary variables of vaccinated and unvaccinated children.

Conclusions

Within the study's limitations, it can be concluded that the vaccinated subjects showed a significantly reduced salivary secretion, pH, and buffering capacity than unvaccinated participants. Most of the vaccinated participants were in the lower buffering category. Based on the findings, it can be inferred that the COVID-19 vaccination may likely to reduce pediatric patients' salivary secretion rate, pH, and buffering capacity and likely to increase the caries risk. Hence, oral health education and preventive dental programs targeted at COVID-19-vaccinated children must be undertaken to avoid oral health consequences.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the research and innovation center of Riyadh Elm University IRB # (FPGRP/2022/704/810/805).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors of this study declare no conflicts of interest.

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