BioMed Research International

The Impact of Lifestyle Factors on Oral Health Conditions

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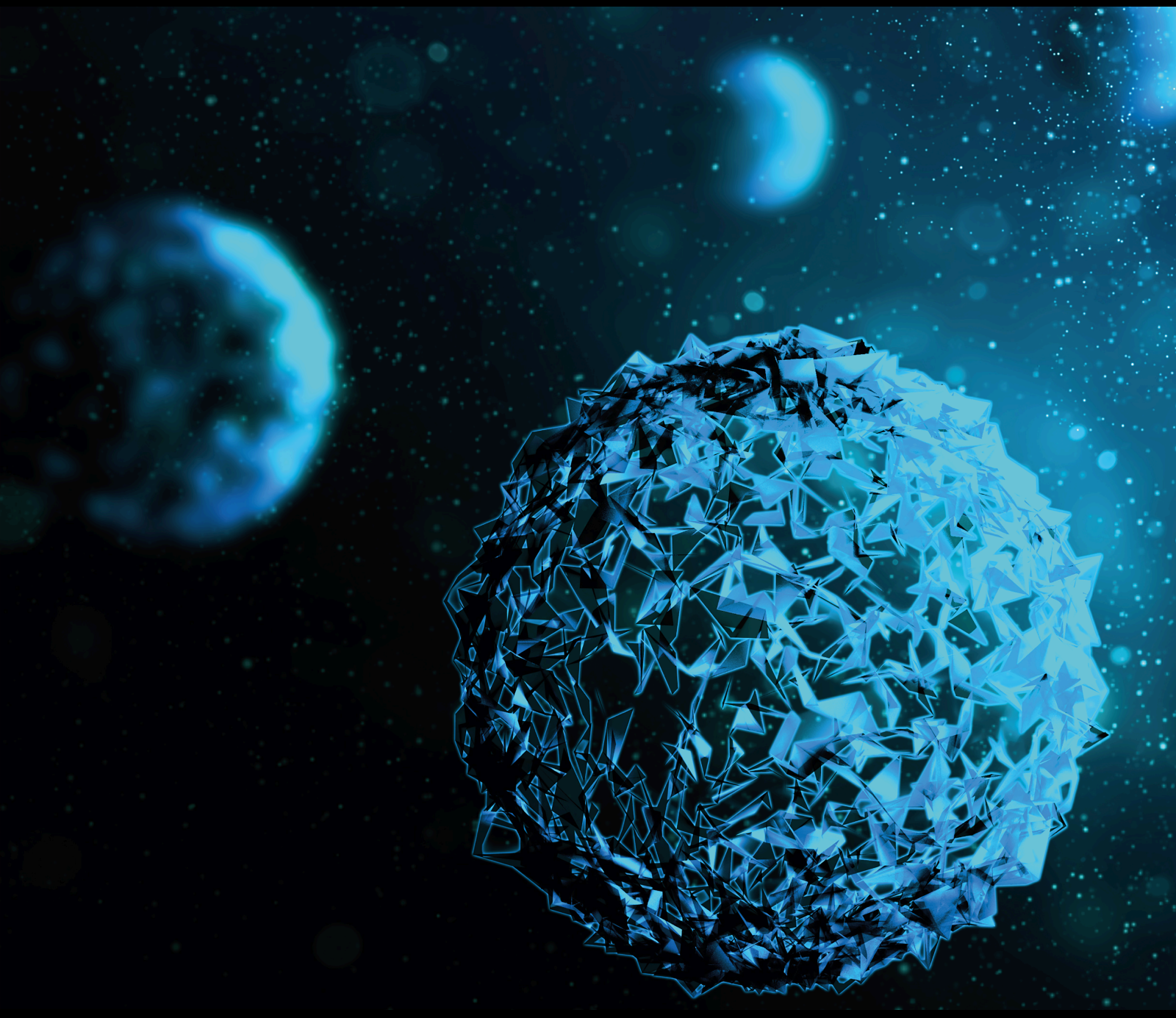

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Research Article

Astaxanthin Enhances Gingival Wound Healing following High Glucose-Induced Oxidative Stress

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Fibroblasts of the gingiva play a key role in oral wound healing in diabetes. In this study, effects of astaxanthin (ASTX), a xanthophyll carotenoid, were tested on gingival fibroblasts in a wound healing assay in vitro. The aim of this study was to determine whether ASTX can recover delayed wound healing or not when oxidative stress is elevated by high glucose exposure. For this purpose, human gingival fibroblasts were incubated with or without ASTX following exposure to systemic doses of low glucose (LG) and high glucose (HG) in culture media (5- and 25-, 50 mM D-glucose in DMEM Ham's F12) following 24 hours of incubation. Levels of ROS (Reactive oxygen species) were determined for each experimental group by confocal microscopy. Cell proliferation and viability were assessed by an automated cell counter with trypan blue assay. Wound healing assay was designed in 60 mm petri dishes. Cells were exposed to 5-, 25-, and 50 mM glucose for 24 hours, and a straight line free of cells was created upon full confluency. 100 μM ASTX was added to the recovery group, simultaneously. Cells were monitored with JuLI®-Br Cell History Recorder. ROS levels were significantly increased with increasing glucose levels, while cell proliferation and viability demonstrated a negative correlation with increasing oxidative stress. ROS levels significantly decreased in the 100 μM ASTX-treated group compared to the gingival fibroblasts treated with 50 mM HG medium-only, as well as growth rate and viability. Wound healing was delayed in a dose-dependent manner following high glucose exposure, while ASTX treatment recovered wounded area by 1.16-fold in the 50 mM HG group. Our results demonstrated that ASTX enhances gingival wound healing through its antioxidative properties following high glucose induced oxidative stress. Therefore, ASTX can be suggested as a promising candidate to maintain oral health in chronic wounds of the oral tissues related to diabetes.

1. Introduction

Diabetes mellitus (DM) is a chronic, metabolic disease in which blood sugar levels increase due to insulin hormone disorders: one of which is hyperglycemia. Hyperglycemia is responsible for various health complications including cardiovascular diseases, retinopathy, neuropathy, and nephropathy [1, 2], as well as impaired oral health due to increasing incidence of periodontal disease in diabetic patients [3–7].

Chronic inflammation of the periodontal tissues is identified as the periodontal disease [4–8]. In diabetic patients, the course of the periodontal disease may be more severe, as high systemic levels of glucose may contribute to increased inflammation [9] and delayed wound healing via impaired cell migration and proliferation [10–12], increased apoptosis [13, 14], and reduced levels of collagen synthesis [15]. In oral mucosa, gingival fibroblasts play a key role in healing process by production and remodeling of the extracellular matrix

(ECM) around the wound tissue [15]. Recently, it has been shown that regeneration capacity of the gingival fibroblasts decreases with increasing concentrations of glucose [16], possibly through a mechanism involving excessive production of reactive oxygen species (ROS) [17].

ROS play a key role in cellular homeostasis via mediation of oxidative stress and inflammation [18, 19]. Low levels of ROS may induce cell cycle arrest, while increased amounts of ROS activate cellular defense mechanisms in vivo. On the other hand, excessive ROS induction is associated with elevated levels of proapoptotic proteins, leading to cell death [20, 21]. Various studies have reported a relationship between oxidative stress and impaired wound healing in chronic, nonhealing wounds due to additional ROS production following prolonged chronic inflammation [22–25]. In diabetic patients with periodontitis, such oxidative damage to cells and tissues of the periodontium is common [22] and has an adverse effect on quality of life [26]. Therefore, reducing the amount of ROS to basal levels is crucial, especially in cases where periodontitis is triggered and/or enhanced by an underlying chronic disease.

On the molecular level, it is possible to prevent these adverse effects through prevention of unwarranted ROS production [27]. Recently, it has been demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid [28], modulates oxidative stress and inflammation through reduction of free radicals [29] and activates endogenous antioxidant systems via genetic modulation [30, 31]. Beneficial effects of ASTX on diabetes, together with or without conventional treatment methods, have been reported [32], including enhanced insulin sensitivity [33, 34], regulation of glucose metabolism [33, 35, 36], and reduction of blood glucose levels [37] in early diabetes, as well as decreased hyperglycemia [37–39], lipid peroxidation, ROS/oxidative stress [40–42], and inflammation [41–45] in diabetes. ASTX is also effective on prevention and treatment of DM-associated pathologies. Positive impact of ASTX has been shown on wound healing in nasal mucosa [46] and vocal fold [47], as well as impaired cutaneous regeneration [48, 49]. However, the effect of the compound on chronic wound healing of the oral mucosa is unknown.

DM is a good model where chronic wound healing is impaired in oral tissues [26]. In this study, an in vitro wound healing assay was designed in gingival fibroblasts following high glucose exposure. The hypothesis tested was that ASTX would reduce levels of ROS induced by high glucose and recover cellular behavior in favor of enhanced wound healing in fibroblasts of the gingiva. Therefore, the aim of this study was to determine whether ASTX can recover delayed wound healing in gingival fibroblasts or not when oxidative stress is elevated.

2. Materials and Methods

2.1. Cell Culture and Experimental Design. All reagents were purchased from Sigma-Aldrich (St. Louis, MO, USA) unless otherwise stated. Human gingival fibroblasts (Accegen Biotechnology, Fairfield, New Jersey, USA, Cat no: ABC-TC3627) were incubated in low glucose (LG) conditions; in a 1 : 1 mixture of Dulbecco's Modified Eagle's Medium/Nutrient Mixture Ham's F-12 (DMEM/F12) containing 10% heat-inactivated fetal bovine serum (FBS), 100 U/ml-μg/ml penicillin-streptomycin (PS), and 2.5 mg/ml amphotericin B (AMP-B) in a humidified atmosphere of 5% CO_2 at 37°C. Cells were counted every 24 hours, and number of dead cells was determined with trypan blue assay with an automated device (Vi-Cell, Beckman Coulter, USA). At the end of the 96th hour, *lag* and *log* phases were determined, and population doubling time (PDT) was calculated as explained in Figure 1(a). Total number of live cells was used for the calculation of growth rate.

Culture media was supplemented with D-glucose and/or ASTX for different experimental setups. D-glucose was added to culture media for a final concentration of 25- and 50 mM. ASTX was dissolved in a 1 : 1 mixture of glycerol and culture media as a stock solution. Smaller volumes were dissolved in culture media to obtain a final concentration of 100 μM.

2.2. Determination of Intracellular ROS Levels. ROS levels were determined for each experimental group by a Leica TCS SP5 confocal microscope (Mannheim, Germany) equipped with 488 nm argon ion and 543 nm green helium neon laser lines. For this purpose, gingival fibroblasts were loaded with 10 μM of cell-permeant 2′,7′-dichlorodihydrofluorescein diacetate (H2DCFDA; Invitrogen, USA) for 60 min at room temperature (RT), as described previously by Tuncay and Turan [50]. A total of maximum fluorescent intensity from 10 random areas within the range of 30-70 cells were measured following 100 μM H_2O_2 exposure and compared to basal fluorescence levels for each cell.

2.3. Determination of Cell Proliferation and Viability. Three replicates for each experimental group were treated with either 5-, 25-, or 50 mM D-glucose. Following 24 hours of incubation, an initial number of 0.02×10^6 cells were cultured in 6-well culture dishes. At the 30th hour of incubation (log phase), 100 μM ASTX was added to 50 mM HG-treated cells. Cells were detached from the culture plate with trypsin-EDTA solution (Biochrom, Germany) for 5 min at 37°C, following another 24 hours of culture to determine final number of viable cells. Cell viability was assessed by Vi-Cell as described above.

2.4. Monitorization of Wound Healing. Gingival fibroblasts were seeded in standard petri dishes and incubated in LG and HG conditions. When cells reached full confluency, a straight line free of cells was created in the midline with a cell scrapper. 25- and 50 mM HG groups were supplied with D-glucose containing media, while 100 μM ASTX was added to the recovery group, simultaneously. Cells were monitored for an additional 48 hours with JuLI®-Br Cell History Recorder (NanoEnTek Inc., Waltham, MA, USA) in "Wound Healing" mode in which the confluency of the central scratch was calculated.

2.5. Statistical Analysis. Results were shown as mean and standard deviation for three experimental replicates. All statistical analyses were performed with an SPSS software

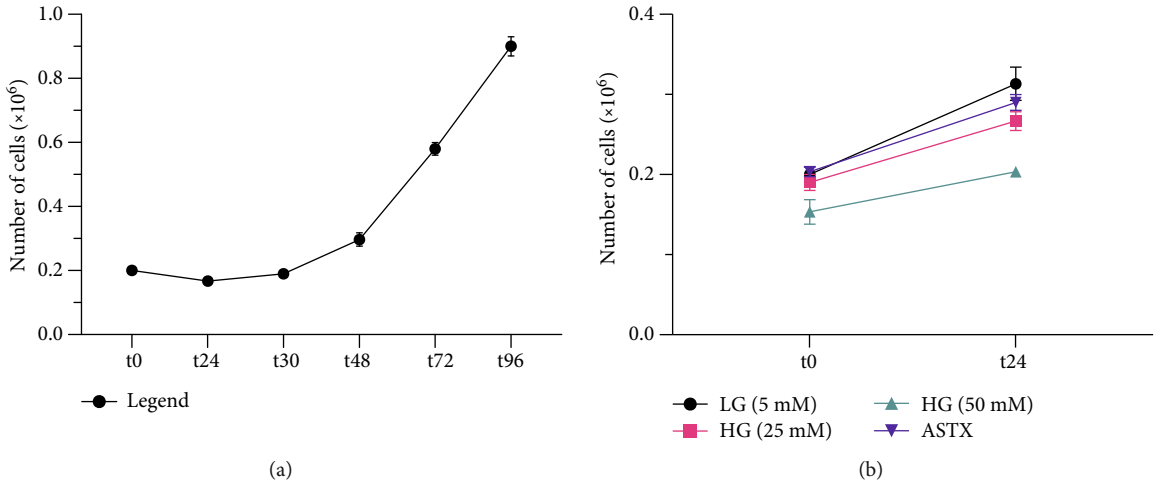

FIGURE 1: (a) PDT was calculated according to the following formula Tln2/ln (Xe – Xb) (T: time in hours since the beginning of the *log* phase; Xb: number of cells at the beginning of the *log* phase; Xe: number of cells at the end of the total time) as 29 hours and 2 minutes following the lag phase at t_{30}. (b) Total number of cells at t_{24} decreased with increasing glucose concentration. Number of cells was recovered by ASTX application following 50 mM HG treatment.

package (SPSS Inc., Chicago, IL, USA). Normally distributed data were analyzed with one-way ANOVA (analysis of variance), and Student's *t*-test was applied to compare groups. The level of significance was $p < 0.05$.

3. Results

3.1. Effects of High Glucose on ROS Levels. To understand the behavior of gingival fibroblasts in LG conditions, a proliferation assay was performed for 96 hours. PDT was calculated as 29 hours, following a 30-hour *lag* phase (Figure 1(a)). Additional glucose and/or ASTX were added following the *lag* phase in subsequent experiments.

To determine the effects of increasing concentrations of glucose on ROS levels, gingival fibroblasts were incubated in 5-, 25-, and 50 mM glucose containing media. Elevated ROS levels were assessed for individual cells via confocal microscopy. ROS levels were increased in a dose-dependent manner (Figure 2(a)). HG treatment induced oxidative stress significantly in both 25- and 50 mM HG groups when compared to the LG group ($p < 0.001$). Representative confocal images were given in Figure 3 for 5-, 25-, and 50 mM HG groups, respectively.

3.2. Effects of High Glucose on Cell Proliferation and Viability. To understand the effects of increasing levels of ROS on cell proliferation, proliferation dynamics of gingival fibroblasts were reevaluated under 25- and 50 mM HG conditions. The LG group was used as a control. Cell proliferation decreased with increasing glucose levels (Figure 1(b)). Growth rate in both 25- and 50 mM HG groups (1.40 ± 0.04 and 1.33 ± 0.1 – fold; $p = 0.0009$ and $p < 0.0001$, respectively) was significantly different than the LG group (1.57 ± 0.04 – fold) (Figure 2(b)).

There was also a negative correlation between ROS levels and cell viability, consistent with the proliferative pattern following HG treatment. The difference between LG ($87.67 \pm 0.58\%$) and 25 mM HG groups ($83.67 \pm 2.31\%$) was not significant ($p = 0.1452$). Percentage of alive cells was significantly lower in the 50 mM HG group ($68.00 \pm 6.00\%$) than the LG group, as well as 25 mM HG group ($p < 0.001$) (Figure 2(c)).

3.3. Effects of ASTX on Impaired ROS Levels, Cell Proliferation, and Viability. To determine the protective effect of ASTX on increasing ROS levels, gingival fibroblasts were incubated for 24 hours in 50 mM HG medium suspended with 100 μM ASTX. ROS levels significantly decreased in the 100 μM ASTX-treated group compared to gingival fibroblasts treated with 50 mM HG medium-only ($p < 0.001$). ROS levels were also significantly different in 100 μM ASTX-treated gingival fibroblasts when compared to the LG group ($p < 0.001$). There was no significant difference between the 25 mM HG group and ASTX-treated group ($p = 0.9432$) indicating a remarkable decline in ROS levels of 50 mM HG treated cells following antioxidant uptake (Figure 2(a)).

Impaired cell proliferation and viability was also recovered by ASTX treatment, when compared to the 50 mM HG group ($p < 0.001$). Levels of growth rate were compatible between ASTX- and 25 mM glucose-treated cells (1.43 ± 0.03 and 1.40 ± 0.04 – fold), in line with ROS levels ($p = 0.2563$). There was a significant difference between LG and ASTX-treated groups when number of cells were compared at 24th hour of incubation ($p = 0.0079$) (Figure 2(b)).

3.4. Effects of ASTX in Wound Healing. Wound healing was determined with JuLI®-BR. At 24th hour of incubation, the wound was healed by 96.00 ± 2.65 percent in the control group. The healed area was significantly decreased in both 25- and 50 mM HG groups ($85.00 \pm 3.00\%$ and 74.33 ± 3.05 %; $p = 0.004$ and $p < 0.001$, respectively), while wound healing was enhanced in ASTX-treated cells ($86.33 \pm 3.05\%$; $p = 0.568$) responsive to the ROS levels (Figure 2(d)). There was also a

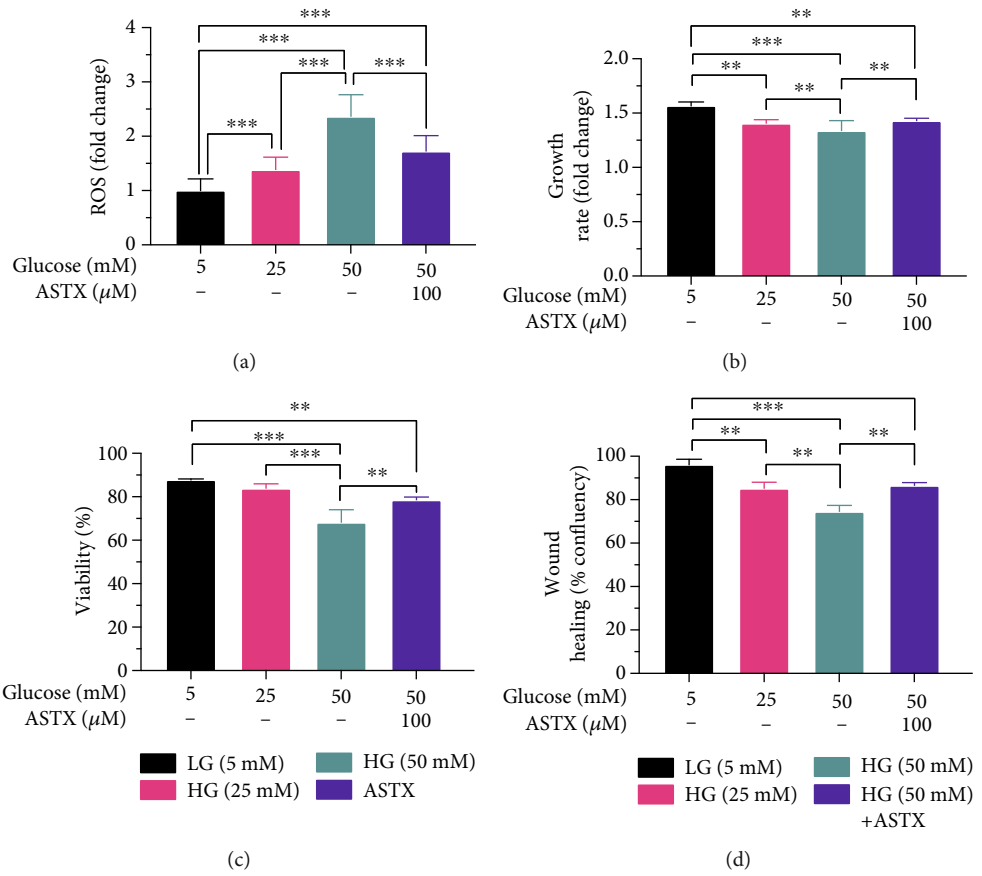

Figure 2: (a) ROS levels were negatively correlated with increasing glucose concentrations, whereas growth rate and cell viability decreased due to intracellular oxidative stress. Oxidative stress in ASTX-treated cells was compatible with the 25 mM HG group, indicating a significant recovery in ROS levels. (b) Growth rate and (c) cell viability were significantly increased following ASTX treatment. (d) Delayed wound healing following increasing ROS levels was recovered following ASTX uptake, due to improved cell proliferation and migration. $^{**}p < 0.005$, $^{***}p < 0.001$. Results were shown as mean and standard deviation for three experimental replicates.

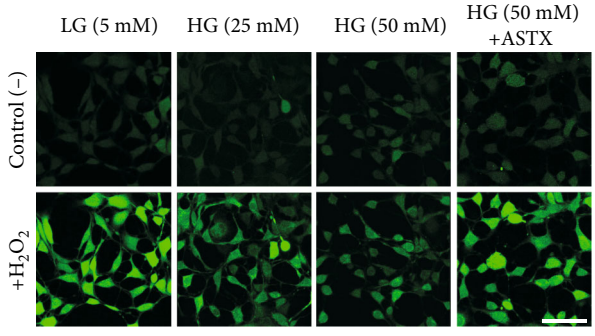

Figure 3: Effects of ASTX on ROS levels induced by hyperglycemia in human gingival fibroblasts were determined by confocal microscopy. Representative images of DCFDA from 5-, 25-, and 50 mM glucose and ASTX-treated groups are given. To monitor the ROS levels, DCFDA loaded cells were calibrated with 100 μM H_2O_2. Changes in total fluorescent intensity in LG group were higher than HG groups, as well as ASTX-treated group ($p < 0.001$). ROS levels were decreased in the ASTX group when compared to the 50 mM HG group ($p < 0.001$). Scale bar: 80 μm.

significant difference in wound closure when the 50 mM HG and recovery groups were compared ($p = 0.002$) (Figure 4).

4. Discussion

Diabetic complications are strongly related to systemic oxidative stress due to high blood glucose levels. One of the most important of these complications is damaged wound closure associated with elevated intracellular ROS [51]. Various in vitro and in vivo studies have confirmed that gingival wound healing is impaired in oral tissues in oxidative stress [52]. Gingival fibroblasts contribute to the regeneration of the gingiva through activation of several genes that have been reported to be involved in tissue remodeling such as control of the cell cycle and proliferation, reorganization of the cytoskeletal proteins, inflammatory response, coagulation, and hemostasis and neoangiogenesis. In this study, an in vitro wound healing model was designed in gingival fibroblasts following high glucose induced oxidative stress. Elevated ROS levels in DM were successfully mimicked in vitro as described previously by Buranasin et al. For this purpose, human gingival fibroblasts were incubated in 5-, 25-, and 50 mM glucose containing culture media for 24

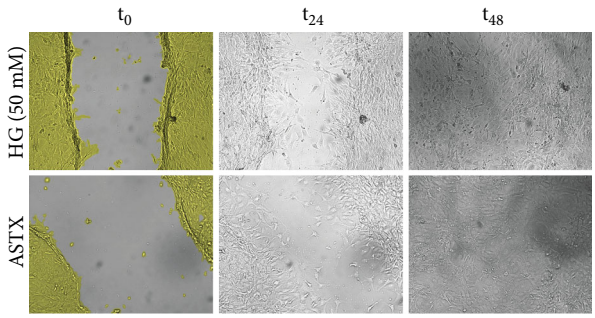

Figure 4: Delayed wound healing in hyperglycemic conditions was impaired following ASTX-treatment. Representative images were from the 24th hour of incubation where confluency was increased by 1.16-fold in ASTX-treated cells compared to the 50 mM HG group ($p = 0.002$). Wounds were closed in both groups at 48th hour.

hours. Application of higher doses was not possible due to total detachment of the cells from the culture plate.

Effects of nonsurgical periodontal treatment along with numerous antioxidants have been inspected in clinical studies. Clinical application of coenzyme Q10 and tea tree oil resulted in reduction of clinical markers of chronic periodontitis [53] where vitamin C had no effect on total antioxidant capacity [54]. Short-term efficacy of lycopene was different from long-term treatment [55, 56], together with zinc and selenium [57]. Although therapeutic potential of individual antioxidants such as NAC, taurine and Thai chi were reported in various studies, ASTX was not listed in any clinical studies investigating periodontal regeneration. However, anti-inflammatory and antioxidative effects of ASTX have been reported in various animal models [41, 43, 58]. Zhuge et al. [59] demonstrated that ASTX significantly reduce blood glucose and total cholesterol levels in a dose-dependent manner in diabetic rats. In another animal study by Mizutani et al. [60], it has been demonstrated that insulin resistance is due to oxidative stress impair cell proliferation and angiogenesis in periodontal repair and destruction. Therefore, we have hypothesized that ASTX would reduce levels of ROS induced by high glucose in gingival fibroblasts and enhance wound healing via improvement of cell proliferation and migration.

In this study, ROS was significantly increased with increasing glucose levels, while growth rate and viability of gingival fibroblasts decreased. ASTX treatment recovered ROS levels, enhanced cell proliferation, and decreased cell death significantly. Lately, it has been showed that ASTX reduces increased levels of hyperglycemia-induced ROS production in mitochondria [61] and inhibits inflammation and apoptosis in several tissues and organs [62]. Buranasin et al. have also reported impaired cell proliferation in hyperglycemic gingival fibroblasts, indicating an oxidative stress mediated mechanism in DM patients with delayed periodontal wound healing. In our study, wound healing was delayed in HG conditions compared to the LG group by 1.15-fold, supporting clinical data by Altingoz et al. [63] where different levels of the same oxidative stress markers were reported in diabetic and nondiabetic patients with periodontitis.

Effects of ASTX have been investigated in several wound tissues including nasal mucosa [46], vocal cord [47] and skin [49]. Topical ASTX application reduced ROS production which prohibited inflammatory cell infiltration in epidermis. In the same study, it was stated that wounds treated with ASTX were completely epithelialized on day 9, while the control group showed only partial epithelialization, delaying complete wound closure by two days [48]. ASTX also reduced large amounts of ROS that is produced during vocal fold healing, resulting in decreased tissue contraction and hyaluronic acid deposition [47]. Alongside with protective effects of ASTX, therapeutic effects were also reported in the postinjury period with significantly decreased subepithelial fibrosis. These results suggest that molecular mechanisms of ASTX are not limited to epithelial healing, but also ECM regeneration in vivo.

In our study, protective effect of ASTX in gingival wound healing was demonstrated for both 25- and 50 mM HG exposure. Impaired growth rate and decreased viability were significantly recovered in ASTX-treated group when compared to the 50 mM HG group. Increased cell proliferation and viability, together with enhanced wound closure, was compatible between the 25 mM HG group and ASTX-treated group, but not with the LG group. Higher doses of ASTX treatment did not improve wound healing further (data not shown), indicating necessity of a diabetic animal model for periodontitis to understand the effects of different systemic doses of ASTX in vivo.

5. Conclusion

Proliferation and migration of the gingival fibroblasts are crucial for periodontal regeneration. However, hyperglycemia impairs wound healing in gingival fibroblasts due to increasing oxidative stress. In this study, ASTX is suggested as a promising candidate to maintain oral health in DM related wounds of the oral tissue through reduction of oxidative stress.

Data Availability

The raw data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Assessment of Oral Health-Related Quality of Life and Its Associated Factors among the Young Adults of Saudi Arabia: A Multicenter Study

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Oral health-related quality of life (OHRQoL) is an essential indicator of people's overall health and health-related quality of life. Poor oral health and OHRQoL among young adults lead to numerous negative consequences and an increased burden on the healthcare system. The present study is aimed at assessing the OHRQoL among the young adults of Saudi Arabia, identifying self-rated oral health, and determining the relationship between sociodemographic and lifestyle factors with the OHRQoL. The present analytical cross-sectional survey was conducted among 1152 health and non-health-related college university students from three randomly selected universities. The OHRQoL was evaluated using the validated Arabic version of the oral health impact profile-14 questionnaire (OHIP-14). Of the population studied, one-fourth of the participants (24.9%) reported poor or fair oral health, and the highest OHIP-14 score was found in the domains of physical pain (4.14), followed by psychological discomfort (4.07). Logistic regression analysis revealed that the poor oral health category was significantly associated with male gender (ref: female: adjusted OR (AOR) = 1.89, 95%CI = 1.23 – 2.94, $p = 0.004$), daily smokers (ref: nonsmokers: AOR = 3.47, 95%CI = 1.97 – 4.82, $p < 0.001$), chocolate and candies intake more than once a day (ref: never; AOR = 1.54, 95%CI = 1.10 – 2.19, $p = 0.034$), and did not seek periodical dental care (ref: periodic dental care received: AOR = 2.23, 95%CI = 1.53-2.86, $p = 0.002$). The present study revealed the factors associated with poor OHRQoL. The concerned authorities should consider the implementation of periodic dental checkups for university students, especially for the high-risk group. Furthermore, it is recommended to have regular health education programs that will help to change the student's lifestyle and poor oral health behaviors.

1. Introduction

Health is "a state of complete physical, mental, and social well-being, not merely the absence of disease and infirmity" as defined by the World Health Organization (WHO) [1]. Oral health (OH) is an essential indicator of people's general health and is closely associated with overall health and health-related quality of life (HRQoL) [2, 3]. HRQoL is an appropriate index for assessing people's overall health and the effect of health conditions on the quality of life [4].

Understanding the health and quality of life leads us to understand the concept of oral health-related quality of life (OHRQoL) [5]. OHRQoL represents the subjective experience of symptoms related to oral conditions that impact the well-being of an individual. The OHRQoL uses patient-centered outcome measures to identify the impact of OH on aspects of everyday life regarding social, psychological, and functional well-being [5, 6]. Poor OH and OHRQoL among people lead to numerous negative consequences, including low self-esteem, depression, decreased performance in daily activities, lack of social interaction, and an increased burden on the healthcare system [3, 7].

Over the past decades, a set of psychometric instruments have been developed to assess OHRQoL [8, 9]. The OH impact profile (OHIP) questionnaire is commonly used to measure OHRQoL in children, adults, and dentate elderly people [10, 11]. The short version of the OHIP includes 14 items (OHIP-14), which are based on Locker's conceptual model to measure OH [10]. These elements represent the consequences of oral diseases and the negative impact they have on OHRQoL. The validity and reliability of OHIP-14 have been shown in many studies, and the instrument has been translated and validated into several languages including Arabic language [9, 12–15]. The factors that affect self-reported OH are not clear, but it has been suggested that oral diseases have a detrimental effect on subjective OH, and that effect is likely to be greater at younger ages. Studies reported that young and middle-aged adults report worse OH than older adults, although oral problems tend to increase with age [16, 17].

In a study conducted by Wei et al. among Japanese students, they reported that young university students are in a dynamic transition period of growth and development that bridges adolescence to adulthood (people in the community) [18]. Many of them start to live away from their homes for the first time in their lives, which can adversely affect their health, lifestyle, and behavior. As a result of these physiological and social changes, their oral health behaviors and their clinical status can quickly deteriorate [18, 19]. Furthermore, poor oral health behaviors, such as high sugar consumption and inadequate brushing habits, may lead to adverse effects on OHRQoL [19, 20].

In the Kingdom of Saudi Arabia (KSA), some authors have attempted to identify the OHRQoL in different settings. Most of the studies that assessed OHRQoL were among patients with a dental problem or elderly participants [14, 17]. Despite the evidence on the importance of OHRQoL assessment among apparently healthy young adults and university students, there is limited data available in the KSA. Considering the necessity of having regional data in this category population, this study was planned to assess the OHRQoL among the young adults of the KSA by using the OHIP-14 questionnaire. The present study is also aimed at determining the relationship between OHRQoL and self-rated oral health among them and to find the association between sociodemographic and lifestyle factors with OHRQoL.

2. Participants and Methods

2.1. Study Description. This multicenter cross-sectional study was carried out among students (aged 18-25) from different colleges (health- and non-health-related colleges) from three universities of the KSA, namely, Jouf University, Northern Border University, and King Saud University.

2.2. Sample Size Estimation. The minimum required participants for this study was estimated based on Cochran's formula for sample size estimation, $n = z^2pq/e^2$. In this formula, $z = 1.96$ in the 95% confidence interval, e is in the 5% error margin, p is the expected proportion, and q is $1p$. Since studies that assessed OHRQoL among the KSA population had depicted huge variations in prevalence in this subject, we have taken a 50% population proportion (p) to obtain a maximum sample size. After applying all the values in Cochran's formula, the estimated minimum required sample for the current survey was 384. The present study included 384 students from each university, and the total estimated sample size was 1152 (3×384).

2.3. Sampling Method. The required number of sample participants was selected by a multistage probability proportional to size (PPS) sampling technique. In this technique, first, two health science colleges and two other colleges were randomly selected using the lot method from each of the three universities. Only a college with both sections (boys and girls) is included. In the following stages, the required number of participants from each college was selected according to gender and year of the students. Finally, the systematic random sampling method was used based on students' university identification numbers to select participants from each year of education.

2.4. Data Collection Method. We have begun the data collection process after ethical approvals obtained from concerned authorities and other necessary administrative permissions. The data collector contacted the selected student during the self-directed learning period with the help of their class leader. After briefly explaining about the survey and getting informed consent, the students filled the data collection form (Google form) in the data collector's electronic device (mobile, tab, or laptop). Only the principal investigator was authorized to access the Google form of the current survey. Students who were not willing to participate or were unavailable during data collection were considered nonrespondents and were replaced by the next student according to the university identification number.

2.5. Data Collection Tool. This research data were collected by using an open-source, structured, and validated self-administered Arabic questionnaire [15] consisting of three parts. The first part inquired about sociodemographic and oral health-related behaviors such as intake of candies, sugary drinks, and brushing teeth. The second part inquired about the participants' perceptions of their oral health by asking through a question "What is your perception of your oral health?," and the responses were recorded from poor to excellent. Finally, we assessed OHRQoL through OHIP-14. The OHIP-14 has 14 questions related to the evaluation of OHRQoL. The responses were recorded in a 5-point Likert scale ranging from never to very often (score is 0 to 4). Then, we calculated the total scores of all domains, and a higher

score indicated poor OHRQoL. The highest possible total score of all the OHIP-14 domains is 56 (14×4). Furthermore, OHRQoL was further categorized into good, for whom score was less than 60% of the total possible score (<35), and poor for whom score was more than or equal to 60% of the total possible score (≥35). The OHIP-14 assesses seven domains in a broad area ranging from functional and social to psychological discomfort caused by their oral health conditions [9, 11]. The present study used an open-source Arabic version of the OHIP-14 tool, validated by Habashneh et al. among Jordanian adults (satisfactory Cronbach's alpha value > 70) [15]. A pilot study was carried out among 30 health and non-health science college students in our region with the adapted Arabic questionnaire. The Cronbach alpha value of the pilot study was 0.89, which exhibited good internal consistency. Hence, the research team proceeded to collect the main study data using this standard and validated Arabic questionnaire.

2.6. Data Analysis. The Microsoft Excel sheet downloaded from Google form was exported to Statistical Package for the Social Sciences (SPSS) version 21. Then, we recoded all the variables in SPSS as per the predefined data coding sheet for further analysis. Descriptive data from this study were presented as frequency and proportion (n; %) for qualitative variables, while quantitative variables were shown as the mean ± SD for age in sociodemographic characteristics. Initially, the research team performed the Shapiro-Wilk test for normality assumption. The Kruskal-Wallis test was applied to find the association between perceived oral health status and OHIP-14 scores. The binomial logistic regression (enter method) analysis was executed to determine the relationship between oral health category status and sociodemographic factors, lifestyle factors, and oral health behaviors. In this enter method, the adjusted covariables were age in years, gender, college type, year of education, smoking status, carbonated drink intake, chocolates, candies consumption, brushing count, and periodic dentist care. This study's statistical tests were two-tailed, and a p value less than 0.05 was set as statistically significant value.

3. Results

Of the 1152 studied participants, the mean (SD) age was 20.98 (1.9), 51.6% were females, the majority (57.5%) were from non-health-related colleges, and more than three-fourth (80.6%) were nonsmokers. Almost a third of the participants were taking carbonated drinks daily (34.8%) and consuming chocolates and candies (34.4%) daily. Regarding oral health-related behaviors, 59.4% of the participants were brushing teeth once a day and a majority (60.1%) of them never visited dental healthcare providers periodically (Table 1).

The participants' responses in each item of the OHIP-14 questionnaire are presented in Table 2. The majority (76.4%) of the study participants never had trouble pronouncing words, two-third (67.1) of the participants never had difficulty doing their usual jobs, and 6.5% of students were self-conscious due to their oral health.

Table 1: Distribution of study participants according to sociodemographic characteristics, lifestyle factors, and oral health behaviors.

Characteristics	Number	%
Age (mean ± SD)	20.98 ± 1.9	
Gender		
Male	594	51.6
Female	558	48.4
College type		
Healthcare-related college	490	42.5
Other colleges	662	57.5
Year of education		
First	303	26.3
Second	240	20.8
Third	233	20.2
Fourth	154	13.4
Fifth	222	19.3
Smoking/shisha habits		
No	928	80.6
Yes: daily	156	13.5
Yes: rarely	68	5.9
Carbonated drink consumption		
Never	152	13.2
Once a day	401	34.8
Seldom/rarely	599	52.0
Consumption of chocolates and candies		
Never	45	3.9
Seldom/rarely	525	45.6
Once daily	397	34.4
More than once a day	185	16.1
Brushing teeth per day		
Once	684	59.4
Twice or more	468	40.6
Visit to the dental provider periodically (every 6 months)		
Yes	460	39.9
No	692	60.1

Figure 1 shows the distribution of mean scores in seven domains of the OHIP-14. Of the participants studied, the highest score was found for physical pain (4.14), followed by psychological discomfort (4.07) and psychological disability (3.73). The mean total score of all seven domains was 24.69 ± 5.2.

Table 3 shows that almost one-third (34.4%) of the participants reported good oral health. Furthermore, the combined OHIP-14 scores the self-rated oral health were assessed by the Kruskal-Wallis (nonparametric) test. Of the sample studied, there was a significant association between self-rated oral health ($p < 0.001$) and pain or discomfort in teeth or gum or mouth ($p = 0.012$) with the OHIP-14 scores.

The participants were further classified into good (<35 of total score) and poor (≥35 of total score) OHRQoL categories. Of the 1152 university students who participated, 197 (17.1%) were in the poor oral health category and 955 (82.9%) were in the good OHRQoL categories (Figure 2). These categories were used for logistic regression analysis.

Table 2: Frequency of responses in each domain of OHIP-14. The data shown below are frequency and proportion; *n* (%).

Domains	Items	Never	Hardly ever	Occasionally	Fairly often	Very often
Functional limitations	Trouble pronouncing words	880 (76.4)	106 (9.2)	108 (9.4)	39 (3.4)	19 (1.6)
	Taste worsened	808 (70.1)	166 (14.4)	139 (12.1)	31 (2.7)	8 (0.7)
Physical pain	Aching mouth	464 (40.3)	354 (30.7)	214 (18.6)	89 (7.7)	31 (2.7)
	Discomfort in eating food	439 (38.1)	291 (25.3)	291 (25.2)	100 (8.7)	31 (2.7)
Psychological discomfort	Being self-conscious	530 (46.0)	206 (17.9)	230 (20.0)	111 (9.6)	75 (6.5)
	Feeling nervous	600 (52.1)	206 (17.9)	213 (18.5)	82 (7.1)	51 (4.4)
Physical disability	Unsatisfactory diet	797 (69.2)	158 (13.7)	118 (10.2)	50 (4.3)	29 (2.5)
	Interrupting meals	651 (56.5)	268 (23.3)	160 (13.9)	44 (3.8)	29 (2.5)
Psychological disability	Embarrassed	609 (52.9)	275 (23.9)	181 (15.7)	63 (5.5)	24 (2.1)
	Difficulty relaxing	607 (52.7)	205 (17.8)	213 (18.5)	72 (6.3)	55 (4.8)
Social disability	Irritable with other people	645 (56.0)	202 (17.5)	195 (16.9)	69 (6.0)	41 (3.6)
	Difficulty doing usual jobs	773 (67.1)	201 (17.4)	118 (10.2)	45 (3.9)	15 (1.3)
Handicap	Life less satisfying	789 (68.5)	164 (14.2)	115 (10.0)	54 (4.7)	30 (2.6)
	Unable to function	790 (68.6)	181 (15.7)	119 (10.3)	38 (3.3)	24 (2.1)

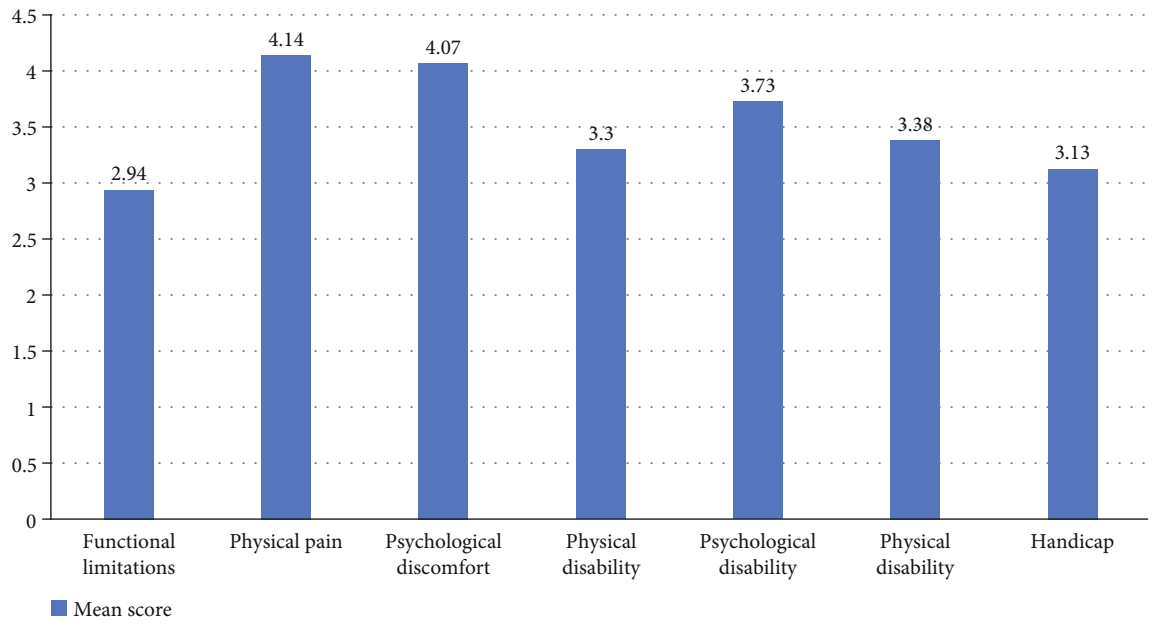

Figure 1: Mean score distribution in different OHIP-14 domains.

The results of binomial logistic regression analysis that was done to find the relationship between oral health category status with the sociodemographic characters, lifestyle factors, and oral health behaviors are presented in Table 4. The poor oral health category was significantly associated with male gender (ref: female: AOR = 1.89, 95 %CI = 1.23–2.94, $p = 0.004$), daily smokers (ref: non-smokers: AOR = 3.47, 95%CI = 1.97–4.82, $p < 0.001$), chocolate and candies intake more than once a day (ref: never; AOR = 1.54, 95% CI = 1.10–2.19, $p = 0.034$), and not seeing the dental care provider periodically (ref: periodic dental care: AOR = 2.23, 95%CI = 1.53-2.86, $p = 0.002$).

4. Discussion

"World oral health day" is observed annually on the 20th of March by the World Dental Federation to reduce the burden of oral diseases. Their campaign theme 2021-2023 focused on inspiring the people on the importance of oral health for its positive effect on general health, well-being, and overall healthy life [21]. This reiterates the importance of assessing OHRQoL among young adults for preventive measures to improve their overall health, as they will be the future of a country.

Table 3: Association between combined OHIP-14 scores with self-rated oral health and pain or discomfort in the mouth*.

Variable	*n* (%)	Mean (±SD)	*p* value
Self-rated oral health			
Poor	179 (15.5)	14.6 (3.7)	
Fair	108 (9.4)	13.3 (2.7)	
Good	396 (34.4)	13.9 (3.4)	<0.001
Very good	346 (30.0)	11.3 (2.7)	
Excellent	123 (10.7)	10.4 (3.2)	
Pain or discomfort in teeth or gum or mouth			
Never	303 (26.3)	11.1 (2.6)	
Rarely	344 (29.9)	11.8 (3.1)	0.012
Sometimes	372 (32.3)	12.8 (3.3)	
Often	133 (11.5)	13.4 (3.8)	

*Kruskal-Wallis test.

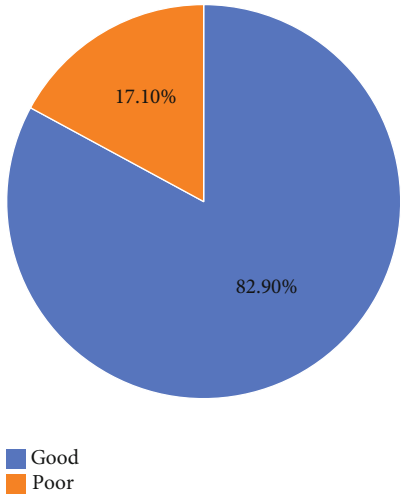

Figure 2: Overall OHRQoL category ($n = 1152$).

Previous researchers worldwide stated that self-rated OH is one of the critical links and predictors of the general health status of the public [22, 23]. The present study findings revealed that one-fourth (24.9%) of the participants perceived their OH status as either poor or fair. A survey conducted by Drachev et al. among Russian university students also revealed similar findings [24]. In contrast, a study done by Moreas et al. has shown a higher proportion of poor self-rated health. This difference in results could be described due to the study settings, inclusion criteria, and methods used. The present study included young adults of both sexes studying at the university, while the latter included only women from a Brazilian community [25]. The present study revealed a positive association between the OHIP-14 scores and self-oral rated health ($p < 0.001$). This study finding is supported by researches of Verhulst et al. and Drachev et al. [23, 24]. Those studies also reported a positive association between perceived poor oral health status and the OHIP-14 scores. These findings again confirm that self-rated oral health is one of the strongest predictors of the OHRQoL and general health.

The results of the current study indicated that the highest OHIP score was found in physical pain, followed by the domains of psychological discomfort and psychological disability domains. Similarly, a study conducted in Jazan city of Saudi Arabia also found that physical pain and psychological discomfort domains had higher OHIP scores than the rest of the domains [14]. Interestingly, a study done by Papaioannou et al. among the Greek population revealed that high scores were determined in functional limitation, physical pain, and handicap domains [26]. This dissimilarity could be justified by the variations in the incorporation of the survey participants. The current study included university students from health and other colleges, while Papaioannou et al. surveyed the adults from rural and urban communities.

On assessing the association between sociodemographic characteristics with the poor OHRQoL, the present study found that male participants had a significantly higher rate of poor OHRQoL (AOR = 1.89, 95%CI = 1.23 – 2.94, $p = 0.004$) than females. However, previously published studies around the world reported different findings. For example, a study done in China by Lu et al. did not find any differences between genders and OHRQoL [27], and a study by Drachev et al. in Russia reported a higher rate of low OHRQoL [24].

This study revealed that poor OHRQoL was significantly higher among the daily smokers (AOR = 3.47, 95%CI = 1.97 – 4.82, $p < 0.001$). Similar to the current study findings, most previous studies also reported a significant association between smokers and poor OHRQoL [28, 29]. Numerous mechanisms explain this striking association between smoking and oral health, including decreased blood flow, increased local edema, and inflammation [30, 31].

Although there are many debates about the periodic screening interval for preventive dental care, the American Dental Association suggested dental screening and evaluation every six months. The current study reported that 60.1% of the participants did not seek dental care providers periodically. The poor OHRQoL was significantly higher among the students who did not visit dental healthcare providers regularly (AOR = 2.23, 95%CI = 1.53 – 2.86, $p = 0.002$). Some researchers have previously evaluated the effectiveness of periodic dental screening [32, 33]. In the KSA,

Table 4: Relationship of the OHRQoL category with sociodemographic characters, lifestyle factors, and oral health behaviors.

Characteristics	Total sample (1152)	Poor OHRQoL		Binomial logistic regression	
		No	Yes	Adjusted OR (95% CI)	p value
Age (mean ± SD)	20.98 ± 1.9			0.958 (0.835–1.09)	0.533
Gender					
Female	558	470 (84.2)	88 (15.8)	Ref	0.004
Male	594	485 (81.6)	109 (18.4)	1.89 (1.23–2.94)	
College type					
Healthcare-related college	490	396 (80.8)	94 (19.2)	Ref	0.108
Other colleges	662	559 (84.4)	103 (15.6)	1.35 (0.94–1.93)	
Year of education					
First	303	259 (85.5)	44 (14.5)	Ref	0.101
Second	240	187 (77.9)	53 (22.1)	0.81 (0.65–1.35)	0.553
Third	233	187 (80.3)	46 (19.7)	1.19 (0.67–2.11)	0.478
Fourth	154	129 (83.8)	25 (12.7)	0.76 (0.58–1.36)	0.688
Fifth/intern	222	193 (86.9)	29 (13.1)	0.85 (0.53–1.41)	
Smoking/shisha habits					
No	928	785 (84.6)	143 (15.4)	Ref	<0.001
Yes: daily	156	116 (74.4)	40 (25.6)	3.47 (1.97–4.82)	0.002
Yes: rarely	68	54 (79.4)	14 (20.6)	2.25 (1.52–2.17)	
Carbonated drink consumption					
Never	152	125 (82.2)	27 (17.8)	Ref	0.128
Seldom/rarely	599	488 (81.5)	111 (18.5)	0.621 (0.34–1.14)	0.916
Once daily	401	342 (85.3)	59 (14.7)	0.971 (0.57–1.66)	
Consumption of chocolates and candies					
Never	45	39 (86.7)	6 (13.3)	Ref	0.969
Seldom/rarely	525	426 (81.1)	99 (18.9)	0.98 (0.75–1.74)	0.317
Once daily	397	325 (81.9)	72 (18.1)	1.23 (0.84–1.98)	0.034
More than once in a day	185	139 (75.1)	46 (23.4)	1.54 (1.10–2.19)	
Brushing teeth per day					
Twice or more	468	403 (86.1)	65 (13.9)	Ref	0.601
Once/never	684	552 (80.7)	132 (19.3)	0.78 (0.56–1.34)	
Visit to the dental provider periodically (every 6 months)					
Yes	460	408 (88.7)	52 (11.3)	Ref	0.002
No	690	545 (78.9)	145 (21.1)	2.23 (1.53-2.86)	

Variable(s) entered on step 1: age in years, gender, college type, year of education, smoking status, carbonated drink intake, chocolates and candies consumption, brushing per day, and periodic dentist care.

the Ministry of Health has established a dental screening program among schoolchildren. However, no structured dental screening program is implemented in university facilities for students.

Despite the best efforts made by the present survey team on this study with a standard methodology, certain constraints are to be noted while reading the findings of the current survey. Firstly, this survey is a questionnaire-based and self-reported. Hence, recall bias, exaggerated responses, and selection bias are to be considered while interpreting the findings of this survey. Secondly, this cross-sectional study attempted to find the association, and not the causation, between the variables.

5. Conclusions

The study findings suggest that self-rated poor oral health is significantly associated with OHIP-14 scores. The present study revealed the factors associated with poor OHRQoL. Physical pain and psychological discomfort were the most common domain with high OHIP scores. The concerned authorities should consider the implementation of periodic dental checkups for university students, especially for the high-risk group. Furthermore, regular health education programs that help change the student's lifestyle and oral health behaviors must be arranged. Finally, an exploratory multicenter study is warranted that compares OHRQoL with the actual oral status of the students.

Data Availability

The data used to support the findings of this study will be provided from **the** corresponding author on request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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