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Control of Somatostatin Receptor 2 (SSTR2) by Proinflammatory, Microbial and Obesity-Associated Signals in Gingival Crevicular Fluid (GCF), Role of Visfatin and Other Adipokines in Obesity with Periodontitis, Besides Diurnal Rhythms-A Systemic Review to Update the Association of Oral Health with Obesity

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Abstract

With the obesity epidemic getting out of control-simultaneous increase in comorbidities is rising as well like type 2 diabetes mellitus (T2DM), metabolic syndrome (MetS) and increased chances of cardiovascular mortality. Hence need of the hour is to control the related causes associated with aetiopathogenesis. Earlier we have emphasized on the role of oral health in obesity. Here we update the information by showing a correlation of presence of somatostatin (SST) in gingival tissues and crevicular fluid (GCF) and how SSTR2 (SST receptor 2) is regulated by proinflammatory, microbial and obesity associated signals in periodontal cells and tissues. With the antiproliferative, antiangiogenic and antiapoptotic actions of SST, SSTR2 might be playing an important role in the aetiopathogenesis of periodontitis. Further we have emphasized on the role of visfatin in aetiopathogesis of obesity and periodontitis besides other cytokines. Role of circadian rhythms and poor lifestyle habits might be responsible especially in children for higher incidence of obesity and periodontitis. Further importance of losing weight emphasizes on how adiponectin improves while tumor necrosis alpha (TNF-α) falls in GCF and helps in curing periodontitis as well. Use of metformin in type 1 obesity was found to be helpful in reducing obesity and periodontitis, reducing the metalloproteinases 1, 3, 8, V that are present in periodontium of obese subjects.

Keywords: *SSTR2; GCF; Visfatin; Adiponectin; Metformin; Periodontitis; Obesity*

Introduction

The incidence of obesity is escalating in mammoth proportions. Association of oral health with obesity and its associated comorbidities like T2DM, metabolic syndrome (MetS) has been well emphasized. Earlier we have reviewed effects of sweetened beverages, other energy drinks high oral sweets associated with chance of periodontitis and dental caries. Moreover Association of type 2 Diabetes Mellitus (T2DM) both in young and old subjects on poor oral health importance of dental doctors in carrying out blood sugars, blood pressure (BP) checking, weight checking has been stressed. Further how important it is to take care of oral health right from birth and how to prevent the effects in newborns, the occurrence of dental problems with feeding habits at night and no sugars left in child's mouth while sleeping has been emphasized. Moreover, we highlighted the importance on the role of salivation in keeping good dental health, along with salivary

molecules as markers for myocardial infarction (MI), cases of uranium poisoning etc. role of beta 3 adrenergic agonists, metals, GWAS studies etc [1-7]. Here we have tried to further update on the other important factors associated with poor oral health and obesity till date.

Methods

We carried out a pubmed search for articles relating to obesity, periodontitis and oral health, using the MeSH terms obesity, T2DM, MetS, periodontitis, oral health, from 2018 till 2019 till date to get an update over the previous articles on the factors correlating with obesity and OH.

Results and Discussion

We found a total of 504 articles, of which we selected 66 articles for this review. No meta-analysis was conducted.

Role of SSTR2

Periodontitis is a highly prevalent chronic inflammatory disease having social, physiological and psychological effects. Progressive along with irreversible damage of tooth supporting tissues, namely periodontium that is made up of gingival, periodontal ligament (PDL), root omentum and alveolar bone [8,9]. For the development and progression of periodontitis organisms of the subgingival biofilm like *Fusobacterium nucleatum* are responsible [10,11]. These microorganisms that are behind the aetiopathogenesis of periodontitis, their parts and products stimulate an inflammatory response in the host, that results in increased amounts of inflammatory mediators like interleukin (IL-) 1β, in gingival tissues and crevicular fluid (GCF). This inflammation results in liberation of matrix-degrading proteases and osteoclast-activating factors, that may end in attachment along with tooth loss [10-12].

Multiple systemic diseases have been known to be correlated with Periodontitis, like type2Diabetes Mellitus (T2DM), obesity along with metabolic syndrome (MetS) [13-15]. The exact aetiology for these interactions is not well understood, partial explanation given is that adipokines might be key for this mechanistic link [16,17]. Increased adipose tissue (AT) is the characteristic of obesity, that means a highly complex and very active metabolic organ is present. Within this AT, adipocytes along with other cells, like leukocytes secrete lot of bioactive molecules, that are named adipokines together [18,19]. Besides controlling metabolism, they also exert control over inflammatory and wound healing processes. Adipokines having pro inflammatory actions are leptin and visfatin. As the leptin secretion is directly proportional to the size, along with number of adipocytes, an increase in plasma leptin results in obesity and gets reduced following weight loss [20]. Similarly, visfatin plasma levels, that is secreted by adipocytes and macrophages get escalated in obese subjects [21,22]. These adipokines can also be measured in the gingival tissues and GCF. Their gingival levels are changed in the presence of periodontitis, that point to a local manufacture and role of these adipokines in Periodontal diseases [23-25].

The polypeptide hormone somatostatin (SST) antagonizes growth hormone (GH) and causes antiproliferative, antiangiogenetic, pro-apoptotic, antinociceptive and other effects [26,27]. Though little is understood regarding the presence, along with actions of SST in Periodontal tissues, few researchers have found SST generating dendritic cells in gingival epithelium along with the sub epithelial connective tissue [28-30]. This SST binds to 5 ubiquitously present G protein coupled receptors GPCR's (SSTR1-5), that are responsible for generating above effects of SST [26]. Activation of SSTR2, that is one of the 5 receptors causes decreased vascular endothelial growth factor (VEGF), insulin like growth factor 1 (IGF1) and their receptors, that have been demonstrated to be key in Periodontal health and repair [31-33]. Moreover, SSTR2 may have importance as a potential target for diagnostic methods in Periodontal bone infection and inflammation [34]. Hence finding the control of SSTR2 may be essential for getting insight in the aetiopathogenesis of Periodontal diseases.

Thus Memmert., *et al.* used *in vitro* human PDL fibroblasts that were exposed to IL-1β, *Fusobacterium nucleatum*, leptin or visfatin. SSTR2 control was checked by real time-PCR and immunocytochemistry. *In vivo*, the SSTR2 expression was evaluated in gingival biopsies of Periodontally diseased along with healthy individuals using real time-PCR and immunocytochemistry. Further the SSTR2 expression

was evaluated in gingival biopsies of rats with ligature induced periodontitis, rats with diet induced obesity (DIO), and periodontally and systemically healthy rats. Statistical analysis was done utilizing, Mann-Whitney-U test and ANOVA with post-hoc tests ($p < 0.05$). Exposure of PDL cells to IL-1β, *Fusobacterium nucleatum* resulted in significant SSTR2 upregulation by 26 times and 6.4 times respectively. Further leptin or visfatin, significantly elevated the SSTR2 gene expression by 3.0 and 2.8 times respectively. Similarly, stimulatory SSTR2 expressions was seen in protein level. SSTR2 expression in human gingival biopsies from periodontitis sites were significantly than those seen in healthy biopsies. Similarly, SSTR2 expression levels were significantly elevated at Periodontally diseased sites in rat experimental periodontitis. Lastly, the SSTR2 expression was significantly upregulated in gingival biopsies of obese rats in contrast to normal weight control animals. Thus, their study gave original understanding regarding SSTR2 control in cells and tissues of the periodontium. They illustrated firstly the proinflammatory, microbial and obesity associated molecules lead to SSTR2 upregulation. As SST has been demonstrated to have antiproliferative, antiangiogenetic, proapoptotic, their study points that SSTR2 might have a crucial role in the aetiopathogenesis of Periodontitis [35].

Role of visfatin

Further as highlighted earlier visfatin is an adipokine which carries essential part in immune functions like growth factor, enzyme, and pro inflammatory mediator. Cetiner., *et al.* aimed to find the amounts of visfatin, IL-6 and TNF-α in GCF in both obese/nonobese subjects with/without generalized chronic Periodontitis (GCF). Patients were divided into obese (O) (n = 31), or nonobese (nO), (n = 19). Further these groups were subcategorized into 4 subgroups as per the Periodontal conditions: i) Periodontally healthy without obesity (nO-Ctrl); ii) GCP without obesity (nO-CP) (See figure 1); iii) Periodontally healthy with obesity (O-Ctrl); and iv) GCP with obesity (O-CP). Demographic data, anthropometric and laboratory data were noted. Periodontal parameters were checked at baseline and 3rd month after either nonsurgical Periodontal therapy or calorie restricted diet therapy. Simultaneously, GCF samples were obtained from subjects to check visfatin, IL-6 and TNF-α amounts. They observed that Periodontal parameters in the O group were significantly more, in contrast to nO groups ($p < 0.05$). IL-6 amounts were in the O-CP group and O-Ctrl, as compared to the nO groups ($p < 0.001$). The visfatin levels of obese subjects were lower following the therapy ($p < 0.05$). Cholesterol amounts were in the O group as compared to nO groups ($p < 0.05$). As compared to other groups visfatin levels were significantly in the O-CP group, but reduced following therapy ($p < 0.05$). Thus, concluding that their results point that visfatin and IL-6 amounts in GCF are correlated with the pathogenesis of obesity and Periodontitis. Within the limits of the study, they thought that there might be a correlation between lipid profile and Periodontitis on systemically healthy subjects [36].

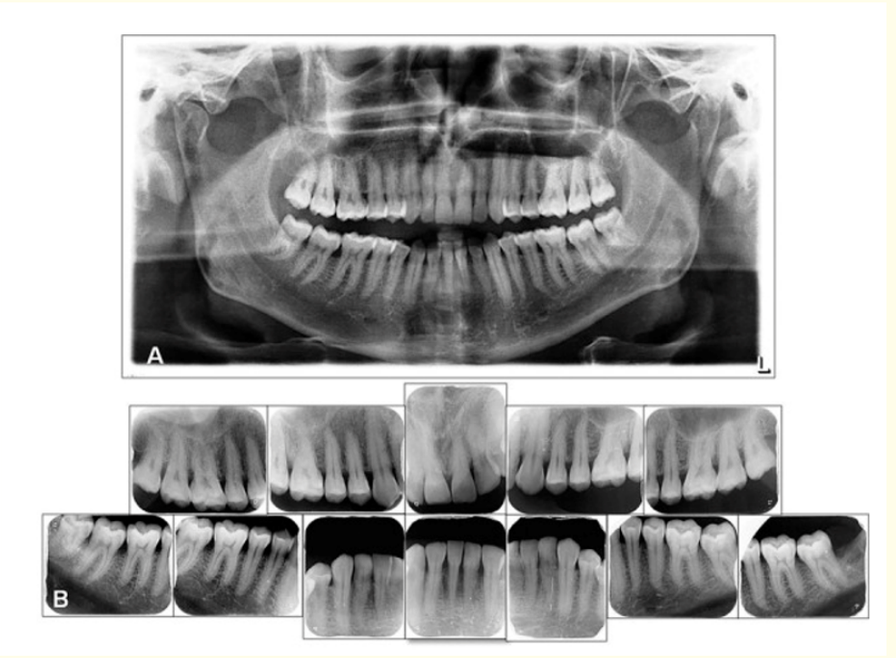

Figure 1: *Courtesy ref no-36. A) Panoramic radiograph of a patient with chronic periodontitis (nO-CP); B) Full mouth periapical radiographs of a patient with chronic periodontitis (nO-CP).*

Role of adiponectin and TNF-α following weight loss

Further Vivekannanda aimed to find the affect of weight loss on the GCF levels of adiponectin and TNF-α in obese subjects with Periodontal disease. They recruited 60 obese subjects who were divided into 3 groups of 20 each. Group-1- Periodontally healthy obese subjects, Group-2- obese subjects with gingivitis, Group-3- obese subjects with Periodontitis. The GCF amounts of adiponectin and TNF-α were checked using ELISA, and the same was associated with probing pocket depth (PPD) and CAL at baseline and following achievement of ≥ 10% weight reduction. Decreases in body weight led to increased adiponectin along with reduction of TNF-α levels in GCF. Significant positive correlation was found with adiponectin levels were seen with improved periodontal parameters in contrast to negative correlation with TNF-α levels. Thus, concluding that weight loss affects obesity-associated inflammatory changes on Periodontal disease. Thus, emphasizing on the importance of weight loss on decreasing the inflammatory burden on the periodontium [37].

Role of IL-23 and IL-35

Periodontitis represents an inflammatory disease of the teeth protecting tissues, caused mostly by gram negative and anaerobes [38,39]. Periodontitis causes progressive degeneration of PDL, with ultimate tooth loss [40]. Gingival plaques contain living bacteria and their biofilm bacteria products like lipopolysaccharides (LPS) induce inflammation. The inflammed then release inflammatory cytokines into the bloodstream as signalling proteins [41]. Conversely DM is known to be a significant risk factor for periodontitis [42]. Persistent hyperglycemia, seen in preDM and DM patients, induce changes in the Periodontal tissue in view of activity of polymorphonuclear leukocytes plus changes in the glycosaminoglycans and cytokines formation. Hence patients with type 2 diabetes mellitus (T2DM) have a high prevalence of gingivitis, Periodontitis, oral candidiasis and xerostomia (dry mouth). Severity of these diseases depends on the duration of the patients DM [43].

Interleukin 23 (IL-23), that is a signalling protein in inflammatory conditions of Periodontitis, also takes a part in mild degrees of DM-associated inflammation [44]. In chronic infections, antigens stimulate dendritic cells, macrophages, and IL-23 synthesis that stimulates the formation of IL-17. Further IL-23 enhances the manufacture of IL-6, IL-1 and tumor necrosis factor α (TNFα) in an autocrine/paracrine pathway [45]. Further IL-35 is an anti-inflammatory cytokine in the IL-12 family that has a suppressive action in the immune system [46]. As IL-23 is responsible for the pathogenesis of T2DM and chronic periodontitis (CP), with controversies in certain studies [47] and absence of data regarding IL-35 role, Maboudi., *et al.* carried out a cross sectional study, in which 72 subjects were divided into 4 equal groups: group A, participants without T2DM and CP; group B, patients with T2DM without CP; Group C patients with CP, but without T2DM and Group D, Patients with T2DM and CP. They obtained detailed demographic information, along with Periodontal conditions, that included clinical attachment loss (CAL), bleeding on probing, plaque index, gingival index and probing depth was analyzed on all existing teeth. Fasting blood sugar (FBS) levels, Haemoglobin A1c (HbA1c), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were evaluated. Additionally, serum IL-23 and 35 were measured utilizing enzyme linked immune sorbent assay (ELISA). Serum levels of IL-23 and 35 demonstrated no significant differences between all groups ($p > 0.05$). There was a significant positive association between the serum concentration of IL-23 along with clinical attachment loss in the control group ($r: 0.548$, $p = 0.019$) was found. A significant negative association between the serum concentration of IL-35 and plaque index in group B ($r: -0.578$, $p = 0.040$), plus significant negative association between IL-23 with ESR ($r: -0.498$, $p = 0.035$) in groups C and D were also found. Thus concluding that inspite of significant correlations of IL-23 and 35 with some Periodontal and inflammatory indices, neither T2DM nor CP differentially alter serum levels of these cytokines [48].

Role of circadian rhythms

Proper timing and sleep duration are essential for our health along with productivity, and irregular lifestyle may sleep disorders and other lifestyle associated health conditions. As per a latest study it was proved that altered daily rhythms cause obesity in adults [49]. As far as oral health and dentistry, daily changes in salivary flow along with content are well understood [50,51]. Salivary flow is low

in the morning, rises in both afternoon and evening and reduces following that. These daily alterations in salivary flow and content are secondary to circadian rhythms, that are endogenous rhythms with a period of roughly 24h [52]. Thus eating at late night, at a time when decreased salivary secretion is present, would cause dental caries easily.

Timing of habits of life like sleep along with meal influences circadian rhythms and circadian rhythms might influence oral functions that are salivary secretion [50,51,53,54]. Hence, irregular sleep or mealtime alters internal circadian rhythms and that appears to lead to irregular salivary secretion and dental caries. This would be applicable in children, since circadian rhythms in developmental periods might get affected by external perturbations [55], that are irregular life habits described differently. As per this posit, associations between life habits and the number of dental caries could be evaluated. Though many publications are there that demonstrate association between the emergence of oral diseases like dental caries and different habits of life [56], most of them concentrated on effects sugar intake, ethnics or rearing surroundings like mother's education [57,58]. Thus Nishide., *et al*. in a study done in University of Japan asked a recording of these life habits for 8consecutive days, namely waking time. bedtime, meal times, snacking frequency, and tooth brushing frequency from 230 children between 1 - 16 yrs old. Evaluation of sleep habits from all information collected along with comparison of dental caries along with life habits utilizing data from subjects with primary (2 - 7 yr of age) or permanent (11 - 16 yrs of age) dentition period. The number of dental caries checked with the use of decay or filled teeth (dft) index associated with bedtime, supper time, regularity of supper time, along with snacking frequency in individuals with primary dentition. Multiple regression analysis showed that bedtime and snacking frequency were mutually independent risk factors for dental caries. There was no correlation between the prevalence of dental caries and other measurement items. Caries number was associated with the regularity of suppertime, and age in subjects with permanent dentition, thus concluding that children with daily life habits correlated with eveningness had a >prevalence of dental caries [59].

Role of TAC and FRAP/nonurate FRAP

Gawron-Skarbek., *et al.* aimed to examine the salivary C-reactive protein and native-urate total antioxidant capacity (TAC) of saliva and plasma in relation to different oral health status indexes in older non-smoking adults. Oral health status involved the Decayed, Missing, Filled Teeth, number of decayed teeth, rough plaque index and community periodontal index with the needs of treatment. 60 old subjects (67.0 ± 4.5 yrs) having separate levels of oral health were evaluated, Salivary CRP was examined as well. The Ferric reducing capacity of saliva/plasma (FRAS/FRAP) and 2.2-diphenyl-1picryl-hydrazyl test of saliva/plasma (FRAS, nonurate FRAS, DPPHS/DPPH) got utilized for evaluating native and non-urate salivary (FRAS, nonurate FRAS, DPPHS, and plasma TAC (FRAP, nonurate FRAP, DPPH, nonurate DPPH). Salivary CRP, native TAC and, nonurate TAC had no relation to any oral health status index. Neither any association was detected for plasma native and nonurate TAC also. Of multiple analysis the only independent predictor of salivary and plasma TAC or CRP protein of saliva. Oral health status indexes were not seen to affect the native or the nonurate local antioxidant status of saliva, or the systemic antioxidant status of plasma they had no local effect associated with CRP. But, lower plasma nonurate antioxidant potential had a correlation with overweight/obesity [60].

Role of pregnancy in obesity and periodontitis

Gomes-Filho., *et al*. tried to examine the correlation between obesity (exposure) and periodontitis (outcome) in pregnant women. Earlier this correlation had been evaluated, where only 5 studies were found to be demonstrating positive correlation. But some of these studies revealed limitations like decreased sample sizes, inadequate exposure criteria and outcome measures, that queries the importance of these studies, Thus a cross-sectional study was done using a sample of 644 pregnant women of the public health service of the municipality of Santo Antonio de Jesus, Bahia, Brazil. Socioeconomic-demographic data, health behaviour, health conditions, along with reproductive history data was compiled with the help of an interview. For obesity, body mass index (BMI) adjusted for gestational age along with expected weight gain. Periodontitis diagnosis used these 2 criteria: i) Center for Disease Prevention and Control and American Academy

of Periodontology (CDC/AAP); ii) Gomes-Filho., *et al.* (2018) using criterion that also examined bleeding upon probing; Prevalence ratios and respective 95% confidence intervals were got by Poisson regression analysis. As per the outcome diagnostic criterion, frequency of periodontitis was 17.24% (Gomes-Filho., *et al.*) and 66.92 (CDC/AAP). Classification of subjects was done as low weight (19.2%), adequate weight (42.39%), overweight (24.84%) and obesity (13.04%), on the basis of exposure diagnostic criterion. The low weight and overweight groups were excluded from the analysis of data, leaving an ultimate total sample of 357 pregnant women. Association between obesity in pregnant women and periodontitis was not statistically significant, after adjusting for confounders like age, schooling level, alcoholic beverage consumption, alimentary and nutritional orientation, urinary infection, and dental flossing. Thus concluding that their findings display a high frequency of periodontitis, obesity and overweight in the studied population but no correlation between obesity and periodontitis in pregnant women was observed [61].

Oral health and periodontitis in Australia

With obesity and periodontitis being a public health in Australia, Khan., *et al.* aimed to find the correlation between obesity and overweight and periodontitis in Australian adults. An evaluation of the cross-sectional data of the National Survey of Adult oral health 2004 - 2006 was performed. BMI calculation, with a self reported questionnaire was utilized for evaluating the estimated par day added sugar consumption. Mean number of sites with probing depth (PD) ≥ 4 mm and CAL ≥ 4 mm and presence of periodontitis were utilized as outcome measures. CDC/AAP periodontitis case definition was used. Bivariate analysis and multivariate variable analysis models were developed. Total of 4317 subjects constituted the study sample. Overweight/obese proportion was 51.9% [95% CI: 48.1, 54.1%], Overall 21.3% (95%CI: 19.3%, 23.5%) people experienced periodontitis. Mean number of sites with PD ≥ 4 mm and CAL ≥ 4 mm were recorded as 0.7 (95% CI: 0.5, 0.9) and 2.4 (95%CI: 2.1, 2.6), respectively. Multiple variable analysis indicated that periodontal parameters [sites with PD) ≥ 4 mm (0.13. 95% CI: -0.86, 0.35) and sites with CAL ≥ 4 mm (0.11, 95%CI: -0.58, 0.35) and presence of periodontitis (1.23, 95%CI: 0.96, 1.57)] were not correlated with overweight/obesity on controlling for; putative confounders. Thus, concluding that a positive association was observed between overweight/ obesity and periodontitis (PD and CAL). But the statistical significance disappeared in the Multiple variable regression analysis, where age, sex, smoking and dental visiting behaviour were observed to be the crucial determinants of periodontitis [62].

Role of smoking and T2DM in periodontitis

As shown earlier Periodontitis represents a multifactorial disease that along with dental caries, is one of the commonest cause of tooth loss all over the world. For efficacious management getting insight into risk factors. Smoking has a dose dependent effect on periodontium. Same way T2DM subjects had severe form of Periodontal diseases. Thus Gupta., *et al*. Aimed to find the prevalence of Periodontal disease in dental pts in association with smoking and T2DM. The study was done in 522 subjects who visited the Periodontitis Department, Kantipur Dental College. Subjects ready to participate signed an informed consent and underwent interview along with clinical examination. Data was collected, on a structured performa, got analysed with the utilization of SPSS 20.0. Periodontitis prevalence was 372 (71.3%). DM33 (6.3%) and smoking as 138 (26.4%). Hypertension was seen in 64 (12.3%) subjects, with family history of DM in 94 (18%). Of the 372 Periodontitis pts, smoking behaviour was present in 120 (16.7%). On the other hand, 120 (87%) smokers, 33 (97%) diabetics, 72 (76.6%) with family history of DM, 62 (96.9%) hypertensive, 216 (41.4%) male and 156 (29.9%) female participants had Periodontitis. Greater smoking behaviour was present in males, 115 (39.4%) as compared to 23 (10%) females. Thus, concluding that Periodontitis was significantly correlated with smoking, DM, hypertension and age. It is recommended that tobacco cessation and DM control needs to be promoted as an integral part of Periodontal therapy and oral health be included as an essential part of general health on concluding national health surveys [63].

Role of high BMI on OTM

Micheloglannakis D., *et al.* tried to examine the effect of raised BMI on orthodontic tooth movement (OTM) and associated factors in children and adolescents. 6 electronic databases and manual searching was done till June 2019 without language along with time restric-

tions. For eligibility it had to be i) longitudinal controlled clinical studies ii) children and adolescents undergoing orthodontic therapy (OT); iii) no systemic diseases; iv) experimental group:patients with enhanced BMI and v) control group: subjects with normal BMI. Screening, study selection along with data extraction were carried out; bias among the studies were checked utilizing the Risk of bias in Non-randomised Studies (ROBINS-1) tool. 7 studied got included. 1 study demonstrated that an enhanced BMI correlated with less wear-time of removable orthodontic appliances, while one study observed no significant correlation. One study documented that BMI was correlated will cooperation during OT; though not seen with the therapy outcomes. One study documented pain experience at the time of OT in adolescents correlated with as compared to those without higher BMI. Two studies illustrated that enhanced BMI in adolescents was associated with OTM, one with higher and one with reduced rates of OTM, respectively. One study documented correlation between enhanced BMI with incidence of white spot lesions and gingivitis at the time of OT. The ROBINS-1 tool demonstrated low to moderate risk of bias within studies. Thus, concluding that the effect of BMI on OTM and associated parameters in children and adolescents remains debatable [64].

Role of updated reviews on relation of overweight/obesity and dental caries in children

Similarly, systematic reviews have demonstrated that any evidence on a link between overweight/obesity and dental caries remains nonconclusive. But this relationship has not been checked for children below 6 yrs of age with primary dentition. Hence an updated systematic review is planned to be conducted by Manohar., *et al*. Studies that will check children < 6 Yrs of age and with complete primary dentition at the time of dental caries check up will be included. Exposure of interest will be the Overweight and obesity status of children < 6 Yrs of age. Outcome will be dental caries in children with complete primary dentition. No restriction on setting, date or language is kept. MEDLINE, Web of Science, Cochrane Central Register of Controlled Trials, Embase, Psyc INFO, ProQuest Central Scopus CINAHL and Google Scholar will be searched for eligible studies. The electronic database search will be supplemented by Open Grey and Grey Literature Report databases. Pro Quest Dissertations and Theses Global, and the International Association for Dental Research conference websites. 2 reviewers will independently screen and select studies, assessed methodological quality and extract data. Meta analysis will be done. If possible Grading of Recommendations Assessment Development and Evaluation (GRADE) Summary of Findings presented. Reg no-PROSPERO CRD 42018085292 [65].

Role of metformin therapy in improving weight loss and periodontitis

Zuniga Curz CA., *et al*. tried to analyse the action of metformin in patients with class 1 obese on t6he activity of metalloproteinases present in the periodontium with chronic Periodontitis. They conducted a clinical study in 68 subjects with class 1 obesity and Periodontal disease. They divided them into 4 groups, 2 of them, in addition to the periodontal therapy, were given metformin 850 mg/day for 6 weeks; 2 samples were obtained/pt of Periodontal tissue before and following each therapy, BMI, plaque index and inflammation were checked. Acrylamide gel zymography was utilized to measure the activity of metalloproteinases in the sample of tissue collected. The results obtained were evaluated by descriptive statistics, student t for related samples and one way- ANOVA was done considering < 0.01 as statistically significant. In the groups of subjects who received metformin at the end of therapy, there was a reduction in BMI, the degree of inflammation and lower metalloproteinase activity as compared to control group (65% vs 25%; < 0.01%). Thus concluding that metformin therapy in patients with class 1 obesity and Periodontal disease, reduces BMI, improves the symptoms of chronic Periodontitis and reduces the metalloproteinases 1, 3, 8, V, present in the periodontium of these patients [66].

Conclusion

Thus, here we have shown how, proinflammatory, microbial and obesity associated molecules lead to SSTR2 upregulation. As SST has been demonstrated to have antiproliferative, antiangiogenetic, proapoptotic, effect study by Memmert points that SSTR2 might have a crucial role in the aetiopathogenesis of Periodontitis and that SSTR2 might be used as a biomarker for Periodontitis. Further role of visfatin and IL-6 in the pathogenesis of obesity and Periodontitis has been emphasized. Although IL-23 and IL-35 had significant correla-

tions with Periodontal and inflammatory indices, neither T2DM nor CP differentially change the serum level of these cytokines. Moreover, weight reduction was shown to improve adiponectin in GCF and decrease TNF-α in GCF in cases of obese subjects with Periodontitis. Further importance of circadian rhythms on the salivary secretion was emphasized, hence late night foods were going to enhance the development of caries hence eveningness needs to be avoided especially in children. No correlation was observed between salivary CRP, Native TAC, and nonurate TAC to any OH status index. Thus OH status indices don't influence native or nonurate local antioxidant status of the saliva, or systemic antioxidant status of plasma; they had no local effect related to salivary CRP. But lower plasma nonurate antioxidant potential correlated with overweight/obesity. Significant association of smoking, T2DM, Hypertension was associated with periodontitis, and hence recommendation of tobacco cessation and T2DM control is needed as an integrated form of periodontal therapy. Moreover, use of metformin in type1 obesity was associated with improvement of obesity along with Periodontal parameters. Rest as highlighted earlier excess sugar sweetened beverages had a bad effect on oral health of children in Australia having poor dental health and with no unequivocal acceptance of causes of childhood obesity and OH an updated systematic review has been planned by the Sydney group. In pregnancy

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