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In Patients with Coronary Heart Disease: Does Oral Hygiene Matter? A Case-Control Study Among Iraqis

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ABSTRACT

Background: Coronary heart disease (CHD) is a leading reason of adult fatality and distress all over the world. Current data have shown that viral and bacterial infections may also contribute to acute atherothrombotic events in susceptible people. Oral illnesses constitute a vital health burden for several countries. Both dental health and periodontal disease (POD) sharing multifactorial etiopathology with CHD. The objective of this work was to inspect the likely association between OHg in patients with CHD among Iraqis and match it to that of healthy subjects.

Material and methods: This are a case-control study, including 118 subjects who had selected from those attending Merjan teaching hospital in Babylon, and the control group included 50 healthy subjects matching the patients as regards sex and age group and had no cardiac problems. **T**he study subjects have examined for their oral hygiene (OHg) in terms of dental caries and periodontal health. The data had analyzed using a computerized SPSS/25 IBM program. A *P*-value of less than 5% had measured as significant. The means and percentages had calculated for the main risk factors. The "Student's *t*-test" had applied to measure the changes between any 2-groups. Meanwhile, the *ANOVA*-test had been used to observe the variations among the groups.

Results: The CHD patients were significantly older than the controls (p-0.05). The males were predominant in this study. The risk factors in terms of hypertension, DM, and smoking history were more among the patients' group ($p<0.05$). All the DMFT-parameters and its breakdown, other than filling teeth, are higher among patients ($p<0.05$). Both grades and stages of POD were significantly worse among the patients compared to healthy subjects ($p<0.05$). There was no significant gender variation among the studied participants regarding all study of OHg parameters. With increasing age, there was a statistically significant worsening of OHg. The subjects who had a positive history of risk factors had a significant worse OHg($p<0.05$).

Conclusion: Poor OHg in terms of dental caries and periodontal status is significantly more in patients with CHD compared to the control group.

Keywords: Dental caries, DMFT index, periodontitis, oral hygiene, and coronary heart diseases

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INTRODUCTION

Coronary heart disease (CHD) is a leading reason of adult fatality and distress all over the world [1-3]. There are well-known risk factors intricated in the pathophysiology of CHD [4, 5]. Current data have publicized that infections may also contribute to acute atherothrombotic events in susceptible people [6]. Oral illnesses constitute a vital health problem for several countries, which affect individuals through their lifespan: causing ache, distress, deformity, and even death. It has predicted that mouth diseases affect approximately 3.5 billion [7]. Both diseases share common predisposing risk-factors with other major non-communicable illnesses [8-10]. Both periodontal and dental statuses had included under the umbrella of oral hygiene (OHg).

Periodontal diseases (POD) constitute a set of inflammatory illnesses in which microbes and/or their by-products are the primary etiologic reasons [9]. Periodontal diseases are widespread, multifaceted, chronic inflammation of the paradental tissue, originated as bacterial biofilm, then flourished mostly by distressed immunity and progressive loss of surrounding gum [11]. A strong correlation of POD has been shown with many organs and systems, including the cardiovascular system [9, 11].

Dental cares have a reversible correlation with and can consider as a crucial factor of OHg. DMFT score is a valuable, informal, and practical measure that can be applied to guesstimate the extent of carious teeth [12, 13]. The impact of poor dental health (expressly in the presence of POD) on the pathogenesis of coronary vessels had supported by a wide range of clinical studies [14]. Both dental health and POD sharing multifactorial etiopathology with CHD [9-11, 14, 15].

The objective of this work was to inspect the likely association between OHg in patients with CHD among Iraqis and match it to that of healthy subjects

METHODS AND MATERIALS

Patients and data selection

This is a case-control study attempt to scrutinize the relationships of the OHg of subjects with CHD set against healthy subjects. The patient group included 118 subjects who had selected from those attending Merjan teaching hospital in Babylon. The diagnosis of CHD had completed based upon medical examination, ECG, and biochemical analyses that justify the definition of CHD (5). The control group included 50 healthy subjects matching the patients as regards sex and age group and had no cardiac problems.

Oral hygiene inspection

Dental status had been inspected using decayed-missed-filled teeth (DMFT)-scoring, which is a WHO-approved index [16] by an expert examiner. The facades of occluded teeth have been cleaned with a soft brush, dried, and checked by tooth-mirror with explorer. The DMFT readings is calculated by [DMF = D + M + F]. The values of DMFT had construed conferring to DMF-scale. Accordingly, DMFT measure of less than 4 reflect the low caries index, measures from 5-9 is moderate, and measures more than 9, considered as high caries index [7, 12, 14]. The research ignores those with complete dental loss (i.e. ''edentulous'').

Evaluation of POD had carried out during the hospital stay. The state of the periodontium had assessed utilizing a standardized probe for measuring the gingival sulcus and also to measure clinical attachment levels (CAL). The entire teeth apart from 3rd molars had examined and clinical data had recorded vis-à-vis: CAL in millimeter, had investigated at 6-sites per tooth [9, 17, 18]. Grading of POD had accomplished based upon ''a new classification outline for periodontial and preimplant diseases: Introduction and key changes from the 1999-classification'' [19]. The participants had divided into 3-grades of POD: healthy-periodontium, localized-POD, and generalized-POD. Likewise, the severity of POD had subdivided according to CAL into 4-stages: healthy-gum (<2mm), mild-POD (2-3mm), moderate-POD (4-5mm), and sever-POD when CAL was >5mm [9, 11].

Statistical Analysis and Ethical Consideration

The data had analyzed using a computerized SPSS/25 IBM program. A *P*-value of less than 5% had measured as significant. The means and percentages had calculated for the main risk factors. The ''Student's *t*-test'' had applied to measure the changes between any 2-groups. Meanwhile, the *ANOVA*-test had been used to observe the variations among the groups.

An informed initial agreement had obtained from every patient (or relative family member) and healthy controls separately. The entire work had approved by the local committee for research ethics at the local authorities.

RESULTS

Baseline characteristics

Table-1 shows a comparison of the baseline characteristics of the enrolled participants between the study groups. The CHD patients were significantly older than the controls (p-0.05). The males were predominant in this study. The risk factors were more among patients' groups, in terms of current smoking, the incidence of hypertension, and DM (p<0.05). All the DMFT-parameters and its breakdown, other than filling teeth, are higher among CHD patients (p<0.05). Along a similar vein, both grades and stages of POD were significantly worse among CHD patients compared to healthy subjects (p<0.05).

Table (1): Comparison of Baseline Characteristics of enrolled participants between the Study Groups

Characters	Patients (*n*=118)	Control (*n*=50)	*P-value*
Age (mean±SD)	59.48 (13.4)	38.46 (11.8)	0.05
Male N (%)	90 (76.3)	41(82)	N >0.05
Female N (%)	28 (23.7)	9 (18)	
Current smokers	29 (24.6)	0	<0.05
Hypertension No (%)	57 (48.3)	4 (8)	<0.05
Diabetes Mellitus No (%)	52 (44.1)	3 (6)	<0.05
Dental Status (mean±SD)			
DMFT	15±10.6	5±5	<0.05
D-T	2.6±3.1	1.6±2.6	<0.05
M-T	11.7±9.2	3.2±3.5	<0.05
F-T	0.6±1.4	0.3±0.7	>0.05
Total	20.6±10.1	27.6±6.2	<0.05
Periodontal Status No (%)			
Grades of Periodontitis			
Normal	19 (16.1)	33 (66)	<0.05
Mild	15 (12.7)	15 (30)	
Sever	84 (71.2)	2 (4)	
Stages of Periodontitis			
Normal	14 (11.9)	1 (2)	<0.05
Mild	45 (38.1)	33 (66)	
Moderate	34 (28.8)	6 (12)	
Sever	25 (21.2)	10 (20)	

Gender variation

There was no significant gender variation among the studied participants regarding all study of oral hygiene parameters (tables 2 and 3).

Table (2): Males & females Differences in DMFT breakdown in all Study Subjects

		Decayed Mean ± SD	Missed Mean ± SD	Filled Mean ± SD	Total Mean ± SD	DMFT Mean ± SD
Gender	**Males**	2.3 ± 3.1	9.4 ± 9.0	0.6± 1.2	23.5 ± 9.0	10.3 ± 7.6
	Females	2.2 ± 2.3	8.6 ± 8.6	0.3 ± 1.4	19.9 ± 11.3	11.3 ± 8.2
P-Value		> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Table (3): Males & females Differences in Periodontitis in all Study Subjects

		Severity			*P-value*	Grading				P-value
		Mild	Normal	Sever		G0	G1	G2	G3	
Gender	**F**	3 (8.1)	14(37.8)	20 (54.1)	>0.05	4 (10.8)	19 (51.4)	9 (24.3)	5 (13.5)	>0.05
	M	27 (20.6)	38 (29)	66 (50.4)		11 (8.4)	59 (45)	31 (23.7)	30 (22.9)	
Total		30	52	86	168	15	78	40	35	

The age in this study has a highly significant impact on all the parameters of OHg ($p<0.05$) except on the filling teeth (p-0.17) as exposed by table-4.

Table (4): Relationships of the age to the oral hygiene parameters of the study subjects

		Dental status					Periodontal Status	
		DMFT	Missing	Decayed	Filled	Total	Severity	Grading
Age	**Pearson Correlation**	0.417	0.4	0.197	0.106	-.516	0.46	0.19
	Sig. (2-tailed)	0.00	0.00	0.011	0.173	0.00	0.00	0.013

To study the relationships of the risk factors of CHD on the study variables, tables (5 and 6) had considered. The subjects who had a positive history of risk factors, in terms of hypertension, diabetes mellitus, and smoking history, had significant ($p<0.05$) higher (worse) DMFT scores (table 5).

Table (5): Relationship of Hypertension, Diabetes, and Smoking to the Classes of DMFT in Study Groups.

Subjects	DMF Classes			Total	*P-Value*
	Less than 4	4-9	More than 9		
Non-Hypertensive	38 (36.2)	20 (19.0)	47 (44.8)	105	< 0.05
Hypertensive	13 (21.7)	8 (13.3)	39 (65.0)	60	
Non-DM	42 (37.5)	20 (17.9)	50 (44.6)	127	< 0.05
DM	9 (17)	8 (15.1)	36 (67.9)	23	
No smoking	31 (40.8)	18 (23.7)	27 (35.5)	76	< 0.05
Ex. smoking	17 (28.3)	3 (5.0)	40 (66.7)	60	
Smoker	3 (10.3)	7 (24.1)	19 (65.5)	29	

Along the same channel, people with a positive history of risk factors had a significant ($p<0.05$) more severe form of POD, which was not the same for grades of POD, in which there were nonsignificant associations (table 6).

Table (5): Relationship of Hypertension, Diabetes, and Smoking to the Classes of Periodontitis in Study Groups

Subjects	Severity of Periodontitis			*P-value*	Grades of Periodontitis				*P-value*
	Normal	Mild	Sever		G0	G1	G2	G3	
Non-Hypertensive	25 (22.1)	44 (38.9)	44 (38.9)	<0.05	10 (9.3)	55 (51.4)	22 (20.6)	20 (18.7)	>0.05
Hypertensive	5 (9.1)	8 (14.5)	42 (76.4)		5 (8.2)	23 (37.3)	18 (29.5)	15 (24.6)	
Non-Diabetic	24 (22.4)	42 (39.3)	41 (38.3)	<0.05	10 (8.8)	54 (47.8)	28 (24.8)	21 (18.6)	>0.05
Diabetes Mellitus	6 (9.8)	10 (16.4)	45 (73.8)		5 (9.1)	24 (43.6)	12 (21.8)	14 (25.5)	
No smoking	14 (17.9)	37 (44.9)	29 (36)	<0.05	6 (7.7)	41 (52.6)	16 (20.5)	15 (19.2)	>0.05
Ex. smoking	10 (16.4)	15 (24.6)	36 (59.0)		7 (11.5)	21 (34.4)	19 (31.1)	14 (23.0)	
Current Smoker	6 (20.7)	2 (6.9)	2 (72.4)		2 (6.9)	16 (55.2)	5 (17.2)	6 (20.7)	

DISCUSSION

The authors hypothesized that poor OHg is associated with a greater risk of CHD. This hypothesis was -to a certain degree- supported by the outcomes of this study. This outcome was in line with numerous earlier meta-analyses and recent surveys, which detected a positive link between CHD and poor OHg [20, 21]. Even though a lack of related indication for the causal-relationship of CHD with POD [22], it is irrefutable that such links are of high importance owing to the possible effect that managing POD could have on decreasing the risk of CHD.

The basic physiopathology that can clarify the association between poor dental hygiene and CAD remains indistinct, even if dental infection may induce a systemic inflammation that contributes to CAD [9, 15]. Furthermore, POD rises the number of circulatory WBCs and systemic values of pro-inflammatory mediators, like C-reactive protein, and uric acid, which have produced in response to cellular damage [11, 23-25]. Of note, several academics provide positive evidence that infrequent growth factors are engaged in the inflammatory process that predates atherogenesis, might be initiated by CRP activity including transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF) [14]. Both TGF-β and PDGF have multicellular activities [26-28]. It has reported that CRP can influence instigation and cross-talk amid ''TLR4 and NF-κB/TGF-β1 signaling-pathway'' that has a dynamic inflammatory role in a cardiac cell-model [14]. TGF-β1 has substantial impacts on periodontial immune response regulation [29]. Similarly, PDGF had observed to be the most systematically deliberated growth-factor in periodontal regeneration [30]. It noted that autogenous CRP might enhance PDGF-β receptor expression and PDGF-mediated chemotaxis. Thus, excite migration of smooth muscle cells that has a recognized role in atherosis [14].

More than 50-carious, infective, and commensal oral organisms, had been determined in thrombotic plaques, and plenty of bacteria links with the oral microbial species of the affected person, signifying that the mouth is one of the bacterial access into the circulation [23]. In this setting, the dental loss is the eventual result of untreated dental illness and a valuable measure of OHg as it mirrors the cumulative impacts of previous diseases and treatments [23]. Additionally, POD progresses gradually and has characterized by chronic inflammatory reaction that causes bony damage, and finally, dental-loss [14, 15]. Besides, dental infection and CAD share same risk factors, like tobacco, DM, and low socioeconomic state [9, 11, 23].

As a rebuttal to this point, it might be convincingly-argued, that no correlation between dental infections and CHD reported by Mattila and associates [31]. In the same way, a current study does not reveal significant changes in the dental status between patients with CHD and control groups [32]. Moreover, the analysis of only non-smokers exhibited a nonsignificant correlation between tooth plaque and total, non-lethal, or lethal cardiac events [23]. In the meantime, Lockhart PB. et al. exposed that patients with CHD revealed poor dental hygiene after adjusting the confounders [33].

The foregoing-discussion implies a heterogeneity of the observed outcomes among the studies that may have caused by the ensuing-aspects. First, diverse diagnostic standards and methods of assessment of POD had practiced. Still, some scholars recorded a link between POD and CHD was constant irrespective of the various parameters as well as the case definitions of POD used [34]. It is indisputable that such variation can lead to disparity in the outcomes. Second, dissimilar types of control peoples had involved amongst the involved research like healthy subjects, trauma patients, and CHD-patients without myocardial infarction had enrolled as healthy control [20, 35]. Third, partial and variant adjustment for confounders may have a role. Some factors can influence both CHD and POD independently, like smoking, DM, and age [35], in addition to the disparities in the socioeconomic status.

Impact of Gender on Oral hygiene and Coronary Heart Diseases

The data of this study appears to suggest that gender displayed no impact on the severity of OHg among the study subjects. A similar phenomenon was also published by other researchers who observed that the association found between POD and CHD is consistent across sexes and independent of the confounders [31, 34]. The premise that young females have better OHg habits compared to males had confirmed by another researcher. Nevertheless, the idea that females have better periodontal status but show higher dental caries than males, not established by the same study [36].

Impact of Age on Oral hygiene and Coronary Heart Diseases

A great deal of data has amassed, in which individuals will get poorer OHg when they age, because poor OHg is strongly associated with increasing age [37]. This was in line with our outcome, which observed a significant association of OHg, with the increasing age. Such finding has expected, owing to the accumulative incidence of dental decaying/loss, POD, concomitant chronic diseases.

Impact of Hypertension on Oral hygiene and Coronary Heart Diseases

Numerous relevant articles focusing on the impact of hypertension on OHg and CHD, have been published. Several studies, including the current works, reporting an association of POD with raised blood pressure [38, 39]. A potential explanation is the proinflammation (that accompanies POD), which denotes a basis for the pathogenesis of CHD. The inflammation can subsidize

endothelial dysfunction, with resultant reduced vasodilation finally leading to changes in the coronary structure [40]. Low-grade inflammation by bacteria and endotoxins, the buildup of oxidative stress, along with molecular mimicry between bacteria and body-antigens, have also been considered as added mechanisms possibly linking POD to systemic illnesses [41].

Impact of Diabetes Mellitus on Oral hygiene and Coronary Heart Diseases

A closer look at the studied subjects revealed a significant association of poor OHg with the incidence of DM, which is in line with numerous other surveys. The association between OHg and DM is intricate and reciprocal [42]. The available data propose that POD may increase the risk of poor glycemic control. Several assumed pathological pathways relating hyperglycemia with OHg, including the stimulated sorbitol-pathway, production of ''advanced glycation end-products'', detrimental influences of oxidative stress, and abnormal lipid breakdown [43]. Other recognized mechanisms may include salivary dysfunction [44] and promoted POD via hyper-inflammatory response to the oral microflora [42]. Of note, it has shown that retinopathy and/or peripheral neuropathy disturbs the hands of diabetic patients may cruelly limit a patient's skull to achieve OHg procedures [45].

To the best of our knowledge, no preceding observational analyses have investigated the link between OHg and the CHD, in Babylon province. Our findings of the association between OHg and CHD could deliver several benefits to community health. This work may have respectable generalizability to other peoples, at best within Iraq. Accordingly, although it might be crucial to consider OHg interferences to preserve good general health, this is dubious -to be effective- for significantly eliminating the risk of CHD, without decrease other risk factors for CHD like smoking, hyperlipidemia, hypertension, diabetes, and lifestyle.

CONCLUSION

Poor OHg in terms of dental caries and periodontal status is significantly more in patients with CHD compared to the control group. risk factors in terms of smoking, increasing age, hypertension, and DM are closely associated with poor OHg status. No significant sex variation was noticed regarding the parameters of OHg among the studied subjects

LIMITATIONS

There are some limitations to this study. There are potential uncontrolled confounders as there is no data concerning diet, the medicine used, and genetic backgrounds, all of which represent a proposed risk factor for poor OHg and CHD. Second, the cross-sectional character of this work disqualifies a decision concerning the causation of the link between OHg and CHD.

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REFERENCES

1. Abed, D.A., et al., *Cystatin-C in patients with acute coronary syndrome: Correlation with ventricular dysfunction, and affected coronary vessels.* Journal of Contemporary Medical Sciences, 2020. **6**(1).
2. A. A. M, H.M.A.-H.M., *Combined Assessments of Multi-panel Biomarkers for Diagnostic Performance in Coronary Artery Disease: Case-Control Analysis.* Sys Rev Pharm, 2020. **11**(6): p. 7.
3. Hajir Karim Abdul-Husseein, F.S.D., Ameera Jasim Al-Aaraji, Hayder Abdul-Amir Makki Al-Hindy, Mazin Jaafar Mousa, *Biochemical causal-effect of circulatory uric acid, and HSCRP and their diagnostic correlation in admitted patients with ischemic heart diseases.* Journal of Cardiovascular Disease Research 2020. **11**(4).
4. Asseel, K.S., et al., *Biochemical Significance of Cystatin-C and High-Sensitive CRP in Patients with Acute Coronary Syndrome; any Clinical Correlation with Diagnosis and Ejection Fraction.* SRP, 2020. **11**(3): p. 301.
5. Al-Mumin A., M.J.M., N. J. Alsalihi, H. A. A. M., *Circulating Atrial Neuropeptides (NT-pANP) vis Cardiac-Troponin (cT-I) After Acute Coronary Syndrome: Relationship with Left Ventricular Ejection Fraction and Number of Affected Vessels by Coronary Angiography.* Biochemical and Cellular Archives, 2020. **20**(2).
6. Beristain-Covarrubias, N., et al., *Understanding Infection-Induced Thrombosis: Lessons Learned From Animal Models.* Frontiers in immunology, 2019. **10**: p. 2569-2569.
7. Organization, W.H., *Oral health, key facts.* https://www.who.int/news-room/fact-sheets/detail/oral-health, 2020. **25-march**.
8. Assembly., U.N.G., *Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Noncommunicable Diseases. .* Resolution A/66/L1. , 2011.
9. Hayder A. A. Al-Hindi, T.A.A.-K., Basim Miteb Zwain, Hussein . A. Al-hamadawi ZA. , *Relationship of Periodontitis with Acute Myocardial Infarction: Case Control Study.* Al-Kufa Univ J Biol. , 2017: p. 11.
10. H. Al-hindi, S.F.A.-S., Basim MH Zwain TAA-KJ., *Relationship of Salivary & Plasma Troponin Levels of Patients with AMI in Merjan medical city of Babylon Province: Cross-Sectional Clinical Study* Al-Kufa Univ J Biol., 2016. **8**(3): p. 6.
11. Samer M. M., A.S.H., Hayder A. Al-Hindy, Mazin J. M., *C-Reactive Protein is Associated with the Severity of Periodontal Disease — An Observational Study Among Acute Myocardial Infarction Patients.* International journal of pharmaceutical research, 2020. **11**(10): p. 252-257.
12. Amir H., M., A. Sahib, B., MH, Zwain et al., *Decayed, Missed, Filled Teeth Scores in Iraqi Patients with Acute Myocardial Infarctio.* Al-Kufa University Journal for Biology, 2016. **8**(3): p. 7.
13. al., K.J.e., *The association between oral health, overall systemic health & age using DMFT score.* T. SJ Oral Sci Health, 2015. **2**(1): p. 16.
14. Raghdan Z. Al-Saad, A.K.S., Fouad Shareef Dleikh, and Hayder Abdul-Amir Makki Al-Hindy, *Is There Any Association Between Highly Sensitive C-Reactive Protein and Dental-Status in Ischemic Heart Diseases? Comparative-Study.* Biochemical and Cellular Archives, 2020. **20**(2).

15. Amir Al-Mumin, H.A.-A.M.A.-H., *Hyperuricemia has a Deleterious Role in Patients with Acute Coronary Syndrome Presented with Poor Oral Hygiene.* International Journal of Pharmaceutical Research, 2020. **Jan-Jun**: p. 7.
16. WHO., *World Health Organization,oral health survey: basic methods.* WHO., 1987. **Third Edition ed: Geneva**.
17. PT., F.A.o., *Report on the Update to the 1999 Classification of Periodontal Diseases and Conditions. .* J Periodontol, 2015. **86**(7): p. 4.
18. Papapanou, P.N.e.a., *Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. .* J Periodontol. , 2018. **89**: p. 9.
19. CatonJ, A., Berglundh T et al. , *A new classification scheme for periodontal and peri-implant diseases and conditions – Introduction and key changes from the 1999 classification. .* J Periodontol., 2018. **89**: p. 8.
20. Shi, Q., et al., *Association between Myocardial Infarction and Periodontitis: A Meta-Analysis of Case-Control Studies.* 2016. **7**(519).
21. Sanz, M., et al., *Periodontitis and cardiovascular diseases: Consensus report.* 2020. **47**(3): p. 268-288.
22. Stewart, R. and M. West, *Increasing Evidence for an Association Between Periodontitis and Cardiovascular Disease.* 2016. **133**(6): p. 549-551.
23. Wilson, K., et al., *Poor oral health and risk of incident myocardial infarction: A prospective cohort study of Swedish adults, 1973–2012.* Scientific Reports, 2018. **8**(1): p. 11479.
24. Maki H. et al. , *On Admission Levels of High Sensitive C-Reactive Protein as A Biomarker in Acute Myocardial Infarction: A Case-Control Study.* Indian Journal of Public Health Research & Development, 2019. **10**(4): p. 5.
25. Al-Hindi et al., *Correlation of on Admission Levels of Serum Uric Acid with Acute Myocardial Infarction: Case-Control Study.* Journal of Global Pharma Technology 2019. **11**(7): p. 6.
26. Fouad S. Dleikh, A.J.A.-A., Rebee M., Mazin J. M., Hayder A. Al-Hindy *Possible cause-and-effect linkage of transforming growth factor-beta1 and platelets derived growth factor-AB with delayed anthropometric parameters in adolescent patients with Cooley's anemia: Cases vis control research strategy.* EurAsian Journal of BioSciences, 2020. **14**(1): p. 7.
27. Makki H., M.M., A. K. S. and Al-Saad R.Z. , *Relationship of levels of transforming growth factorbeta1 (TGF-β1) to the levels of ferritin in blood of transfusion dependent β-thalassemia major patients with growth retardation: A case-control study.* EurAsian Journal of BioSciences, 2020. **14**(1): p. 10.
28. H. A. A., M.M., Shaker A., *No Significant Relationship of Ferritin Levels to the Levels of Platelet-derived Growth Factor (PDGF) in the Peripheral Blood of Transfusion-dependent β-Thalassemia Major Patients with Growth Retardation.* Int J Pharm Res, 2020. **12**(3): p. 8.
29. Gürkan, A., et al., *Gingival crevicular fluid transforming growth factor-β1 in several forms of periodontal disease.* Archives of oral biology, 2006. **51**: p. 906-12.
30. Thakare, K., et al., *Periodontal regeneration using platelet-derived growth factor in infrabony defects: a series of three cases.* Case reports in dentistry, 2013. **2013**: p. 849823-849823.
31. Mattila KJ, V.M., Nieminen MS, Valtonen VV, Hietaniemi KL., *Dental infections and coronary atherosclerosis.* Atheroscle rosis 1993. **103**: p. 7.
32. Beatriz Gonzalez-Navarro, E.J.-S., Jose Lopez-López, X. P.-S. , *Is There a Relationship between Dental and/or Periodontal Pathology and Values of C - reactive protein, Homocysteine and Lipoprotein (a) in Patients with Cardiovascular Disease? A Case Control Study.* Journal of Current Medical Research and Opinion, 2020. **3**(5): p. 8.
33. Lockhart PB, B.A., Papapanou PN, et al., *Periodontal disease and atherosclerotic vascular disease: does the evidence support an independent association?: a scientific statement from the American Heart Association.* Circulation, 2012. **125**: p. 25.
34. Andriankaja, O.M., et al., *Periodontal disease and risk of myocardial infarction: the role of gender and smoking.* Eur J Epidemiol, 2007. **22**(10): p. 699-705.
35. Kodovazenitis, G., et al., *Periodontal disease is associated with higher levels of C-reactive protein in non-diabetic, non-smoking acute myocardial infarction patients.* J Dent, 2011. **39**(12): p. 849-54.
36. Mamai-Homata, E., H. Koletsi-Kounari, and V. Margaritis, *Gender differences in oral health status and behavior of Greek dental students: A meta-analysis of 1981, 2000, and 2010 data.* Journal of International Society of Preventive & Community Dentistry, 2016. **6**(1): p. 60-68.
37. Renvert, S., R.E. Persson, and G.R. Persson, *Tooth loss and periodontitis in older individuals: results from the Swedish National Study on Aging and Care.* J Periodontol, 2013. **84**(8): p. 1134-44.
38. Pietropaoli, D., et al., *Poor Oral Health and Blood Pressure Control Among US Hypertensive Adults.* 2018. **72**(6): p. 1365-1373.
39. Martin-Cabezas R, S.N., Petit C, Agossa K, Gaertner S, Tenenbaum H, Davideau JL, Huck O. , *Association between periodontitis and arterial hypertension: a systematic review and meta-analysis.* Am Heart J. , 2016. **180**: p. 14.
40. Pietropaoli, D., et al., *Poor Oral Health and Blood Pressure Control Among US Hypertensive Adults.* Hypertension, 2018. **72**(6): p. 1365-1373.
41. Chhibber-Goel J, S.V., Bhowmik D, Vivek R, Parakh N, Bhargava B, Sharma A. , *Linkages between oral commensal bacteria and atherosclerotic plaques in coronary artery disease patients.* NPJ Biofilms Microbiomes, 2016. **2**: p. 7.
42. Taylor, I.B.L.E.L.W.S.B.G.W., *The relationship between oral health and diabetes mellitus.* JADA, 2008. **139**: p. 6.
43. Lalla E, L.I., Feit M, et al., *Blockade of RAGE suppresses periodontitis-associated bone loss in diabetic mice. .* J Clin Invest, 2000. **105**(8): p. 9.
44. Moore PA, G.J., Etzel KR, Weyant RJ, Orchard T., *Type 1 diabetes mellitus, xerostomia, and salivary flow rates.* Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001. **92**(3): p. 11.
45. JA., S., *Diabetes and oral health: an overview.* JADA, 2003. **134**.