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Effectiveness of Periodontal Therapy on Liver Function Tests in Systemically Healthy Chronic Periodontitis Patients

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Abstract **Original Research Article**

Periodontitis and liver diseases significantly influence the health. Numerous studies were investigated the relationship between periodontitis and hepatic diseases. The purpose of the present study designed to evaluate the effect of non-surgical periodontal therapy on serum levels of several liver function tests in systemically healthy individuals. Twenty moderates to severe chronic periodontitis (CP) patients (diseased group) and fifteen periodontally healthy subjects (control group) were involved in present research. The diseased group evaluated clinically by the following: Plaque and Bleeding Index (PI, BI), Pocket depth (PD) and Clinical Attachment Level (CAL) at baseline and 1 month after periodontal treatment. Serum levels of liver function tests; Total protein (TP), Albumen (ALB), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP) plus to direct and total Bilirubin (BIL-D and BIL-T) were analyzed for all diseased and healthy participants. Statistical analysis revealed highly significant improvement of clinical parameters (BI, PD, CAL) ($P<0.01$) and significant difference for (PI) ($P<0.05$) when comparing the baseline to 1 month after periodontal therapy. Biochemical assaying showed enhancement in levels of all liver function tests at 1 month versus to baseline of treatment, highly significant differences for TP ($P<0.01$) and significant differences for ALB ($P<0.05$), the other tests became non-significant ($P>0.05$). When comparing of diseased group at baseline versus healthy control subjects, the TP and ALB appeared highly significant differences ($P<0.01$), the other tests increased in diseased patients than healthy subjects but the differences are non-significant ($P>0.05$). Furthermore, there was a significant correlation ($r= -0.562$) between PD and TP only at 1 month after initial therapy. The obtained results suggested that the periodontal therapy might had a beneficial effect on liver health. Further researches needed to clarify the effectiveness of periodontitis and periodontal therapy on health and diseased hepatic patients.

Keywords: Periodontal, Therapy, Liver, Function Tests, Chronic Periodontitis.

INTRODUCTION

Periodontal diseases comprise a number of diseased conditions that affect the periodontal tissues result in attachment loss and destruction of alveolar bone [1]. The major periodontal pathogens associated with periodontitis include the gram-negative anaerobes; *Porphyromans gingivalis*, *Trepanoma denticola* and *Tanerella forsythia* together which famous as the "red-complex" of bacterial groups [2]. Periodontitis had a local effect that leads to loss of teeth [3], in addition to the potential pathologic impact on the systemic status of the human [4].

Numerous studies have confirmed the association between periodontitis and systemic diseases, such as diabetes, respiratory diseases, osteoporosis and cardiovascular diseases. Increasing evidence also indicated that periodontitis may participate in the progression of liver diseases, such as non-alcoholic fatty liver disease, hepatocellular carcinoma and cirrhosis, as well as affecting liver transplantation [5-7].

A study examined an association of periodontal status with liver abnormalities and metabolic syndrome [8], the authors concluded that periodontal disease may be further aggravated by the existence of liver abnormalities and metabolic syndrome in Japanese middle-aged males with low alcohol consumption.

Periodontitis might progress the liver status through the presence of the possible mechanisms

include; bacteremia of the periodontal pathogens, pro-inflammatory mediators and oxidative stress [5]. Bacteria also have a negative effect on the liver, it is well known that patients with cirrhosis are at greater risk of bacterial infection [9, 10] and infections rate is 4 - to 5-fold higher than the general population [11, 12]. Infection with high-virulence *P. gingivalis* might be an additional risk factor for the development and progression of non-alcoholic fatty liver disease (NAFLD). In vitro study, *A. actinomycetemcomitans*detected in liver tissue after intravenously inoculating mice with live *A. actinomycetemcomitans* and possible to induced hepatic moderate inflammation. The inflammatory effect of *A. actinomycetemcomitans* exhibited severe inflammatory effects in the liver, that positively associated with increased serum of inflammatory markers, such as interleukin- 1β (IL-1β), IL-6, IL-10, IL-12, interferon-γ (INF-γ) and tumor necrosis factor-α (TNF-α) [13].

The pathogenic periodontal microorganisms stimulate the periodontal tissues to produces numerous an inflammatory cytokines such as; IL-1β, IL-6, IL-8, IL-12, TNF-α and γ, monocyte chemotactic protein 5 (MCP-5), macrophage inflammatory protein-1α (MIP-1α), prostaglandin (E2) and nitric oxide (NO) [14, 15]. These pro-inflammatory cytokines are involved in the progression of liver diseases as cirrhosis [6].

Expression of pro-inflammatory cytokines in the liver and spleen after oral administration of *P. gingivalis* in mice recently investigated by Ren *et al*., [16], they reported that, liver and spleen tissue of *P. gingivalis* treated mice had higher mRNA and protein levels of pro-inflammatory cytokines compared to the control group. The production of proinflammatory cytokines in the liver and spleen was therefore suggested to increase as a result of oral administration of *P. gingivalis* in mice and may provide further understanding of the mechanisms linking periodontitis and systemic disorders.

Reactive oxygen species (ROS), including superoxide, hydrogen peroxide and hydroxyl anions, are products of normal cellular metabolism. The production of ROS is an essential protective mechanism against diseases associated with phagocytic infiltration as the host defense against bacterial pathogens [17]. However, overproduction of ROS oxidizes DNA, lipids and proteins that contribute to tissue damage [18]. With the progression of periodontitis, ROS produced by periodontal inflammation diffused into the blood stream [19]. Such a condition caused the oxidation of various molecules in blood leading to circulating oxidative stress, which may gradually injure multiple organs [20].

There are little available trails on the efficacy of periodontal therapy on the systemic levels of liver function tests especially in systemic healthy individuals. The tooth brushing promoted healing of periodontal tissues decreased serum lipopolysaccharide concentration and suppressed liver injury in a rat periodontitis model [21]. The microvesicular steatosis caused by periodontitis in rats is reversible after removal of the ligature, which is associated with the increase in oxidative stress and lipid peroxidation in the liver [22].

In other experimental study, scaling and root planing (SRP) could improve insulin resistance and mRNA levels of hepatic CD36 were all significant decreased after 2-weeks of periodontal therapy [23].

Effect of SRP on liver function tests of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in systemically healthy chronic periodontitis subjects studied by Khatavkar *et al*., [24]. They reported that a statistically significant difference between mean AST & ALT levels at baseline and after 1–months of initial therapy was found [24].

Regarding to the previous knowledge, the present study aimed to investigate the effectiveness of periodontal therapy on the levels of the following liver function testes; direct and total Bilirubin (BIL-D and BIL-T), ALT, AST, Alkaline phosphatase (ALP), Albumin (ALB) and Total protein (TP), in systemically healthy chronic periodontitis patients.

MATERIALS AND METHODS

Patients

Thirty-five male individuals aged between 25-58 years selected from Umm Al-Qura Dental Teaching Hospital after ethical approval, and informed consent taken and examined in Periodontics Department Clinic. They participants categorized into two groups: Group 1 (20 moderate to severe CP patients (37.13±7.16) and Group 2 (15 healthy subjects, with mean age (29.6±4.92). The inclusion criteria of the patients are systemically healthy according to Cornell medical index [25], and non-smokers.

Periodontal Examination

The periodontal condition of each patient was measured by using of the following clinical parameters: probing pocket depth (PD), clinical attachment level (CAL) [26], plaque index (PI) [27] and bleeding index (BI) [28], before and after periodontal treatment.

Blood Samples

5 ml of peripheral blood taken from the anticubital fossa by venipuncture using 20 gauge needles with 5ml syringes at baseline and after periodontal therapy (one month). Blood specimens left to clotting for about hour, and then centrifuged to collect the serum. The serum samples separated in Eppendorf tubes and stored at -80 °C until analysis.

Biochemical Analysis

The biochemical indices has been determined in serum using a UV/Vis spectrophotometer (Humastar 200, automatic biochemistry analyser, Wiesbaden · Germany). The level of serum albumin (ALB) had determined by the bromocresol green method. Total protein content of the samples assayed by the Biuret method [30]. Bilirubin estimated by the method described by Jendrassik and Grof [31]. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) was determined [32], alkaline phosphatase (ALP) by the phenolphthalein monophosphate method [33]. The biochemical assaying of these tests by using commercial human kits.

Periodontal Therapy

The non-surgical periodontal therapy done for all patients after measuring of the all-clinical parameters. The periodontal treatment includes; removing of supra and subgingival calculus using an ultrasonic device and Gracey curettes on two visits. In addition, the motivation and advises of oral hygiene instructions were introduce to all patients; by applying Listerine® (McNeil division of Johnson & Johnson company) mouthwash and using toothbrush three times daily and other cleaning devices.

STATISTICAL ANALYSIS

Statistical analysis done by using SPSS (statistical package for social science) program version 21. The obtained quantitative data presented in the following mean and standard deviation. Paired and unpaired t-test used to analyze quantitative data; in addition, Pearson′s correlation used to study correlation between periodontal indices versus to levels liver function tests. Significance considered when P value ≤ 0.05. The statistical data tabulated and graphed by using Microsoft-word 2015.

RESULTS

Clinical Parameters

The mean values of periodontal parameters; PI, BI, PD and CAL improved at 1 month versus to the baseline in CP patients. The statistical analysis revealed that the PI was significantly decreased (P<0.05), while the statistical comparisons of other parameters were highly significant (P<0.01) Table-1.

Serum Levels of Liver Function Tests

The serum levels of the following liver function tests; TP, ALB, ALP, AST, ALT, BIL-D and BIL-T detected in chronic periodontitis patients (baseline and 1 month) after periodontal therapy, in addition to the healthy control subjects Table 2-4.

The mean values of liver function testes for chronic periodontitis and periodontal healthy subjects were within the normal references according the manufacture assaying kits.

The mean values of TP and ALB were improved and increased after periodontal therapy. The statistical comparisons revealed that a significant difference for ALB (P<0.05), but the difference was highly significant for TP (P<0.01). Regarding to comparisons between baseline and control levels, the statistical analysis was highly significant (P < 0.01), on the other hand, there were non-significant differences between the levels of TP and ALB in 1 month after treatment versus control (P<0.05) Fig-1.

Concerning the levels of AST, ALT BIL-D were decreased and the others; ALP and BIL-T were slightly increased after periodontal therapy. The statistical analysis observed that non-significant differences (P<0.05), also, the comparison between both baseline and 1 month compared control levels displayed non-significant differences (P<0.05) Fig 2 & 3.

Pearson's correlation for clinical parameters and liver function tests analyzed for stages; baseline and 1 month after periodontal treatment in chronic periodontitis patients. The statistical analysis stated non-significant correlations. For exception, there was a mild significant correlation observed between PD and TP after 1 month in periodontitis patients. Table 5 & 6.

Table-1: Demonstrate the statistical comparisons of clinical parameters in the diseased group before and after periodontal therapy

	Comparison	Mean ± SD	T value	P values
PI	Baseline	(45.64±16.20)	2.484	0.026*
	1 Month	(38.27±13.18)		
BI	Baseline	(46.34±14.20)	3.570	0.003**
	1 Month	(36.04±15.22)		
PD	Baseline	(2.61±0.62)	3.205	0.006**
	1 Month	(2.33±0.48)		
CAL	Baseline	(2.39±0.51)	2.703	0.017**
	1 Month	(2.21±0.53)		

Table-2: Showed the comparisons of mean values for liver functions tests in the diseased group before and after periodontal therapy

	Comparison	Mean ± SD	T value	P values
TP	Baseline	6.68±0.45	-4.094	0.001**
	1 Month	7.28±0.38		
ALB	Baseline	4.21±0.25	-2.855	0.013*
	1 Month	4.52±0.34		
ALP	Baseline	58.86±10.56	-1.895	0.079
	1 Month	68.06±17.84		
AST	Baseline	23.86±10.55	0.365	0.721
	1 Month	22.86±8.65		
ALT	Baseline	26.46±15.34	0.506	0.621
	1 Month	24.06±15.99		
BIL-D	Baseline	0.19±0.12	1.567	0.140
	1 Month	0.15±0.07		
BIL-T	Baseline	0.43±0.30	-.860	0.405
	1 Month	0.51±0.21		

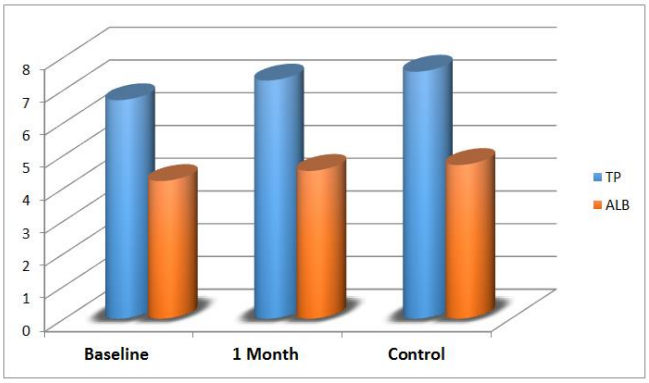

Fig-1: Demonstrate the serum mean values of Total protein and Albumin in diseased group at baseline and 1 month, and healthy control subjects

Table-3: Revealed the statistical comparison for the mean values of liver function tests before periodontal treatment in diseased patients compared to healthy control subjects

	Mean ± SD	T value	P values
TP	Baseline (6.68±0.45)	-5.580	0.000**
	Control (7.55±0.40)		
ALB	Baseline (4.21±0.25)	-4.427	0.000**
	Control (4.70±0.34)		
ALP	Baseline (58.86±10.56)	-1.835	0.077
	Control (65.93±10.52)		
AST	Baseline (23.86±10.55)	1.307	0.202
	Control (19.93±4.94)		
ALT	Baseline (26.46±15.34)	0.865	0.394
	Control (21.46±16.30)		
BIL-D	Baseline (0.19±0.12)	0.720	0.478
	Control (0.16±0.11)		
BIL-T	Baseline (0.43±0.30)	-0.792	0.435
	Control (0.53±0.38)		

Table-4: Express the statistical analysis of the mean values of liver function tests after periodontal therapy opposite to healthy control subjects

	Mean ± SD	T value	P values
TP	1 Month (7.28±0.38)	-1.91	0.066
	Control (7.55±0.40)		
ALB	1 Month (4.52±0.34)	-1.419	0.167
	Control (4.70±0.34)		
ALP	1 Month (68.06±17.84)	0.399	0.693
	Control (65.93±10.52)		
AST	1 Month (22.86±8.65)	1.139	0.264
	Control (19.93±4.94)		
ALT	1 Month (24.06±15.99)	0.441	0.663
	Control (21.46±16.30)		
BIL-D	1 Month (0.15±0.05)	-0.454	0.653
	Control (0.16±0.11)		
BIL-T	1 Month (0.51±0.21)	-0.177	0.861
	Control (0.53±0.38)		

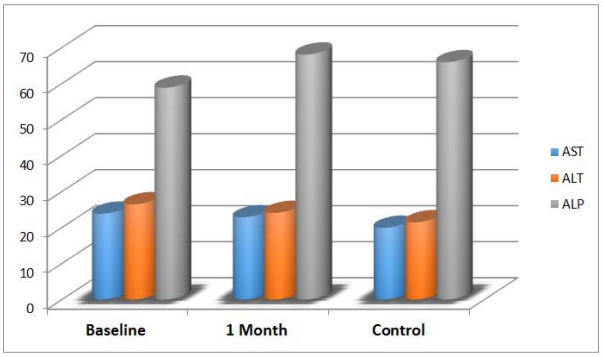

Fig-2: Exhibit the serum levels of AST, ALT and ALP in chronic periodontitis patients at baseline and 1 month, and healthy control subjects

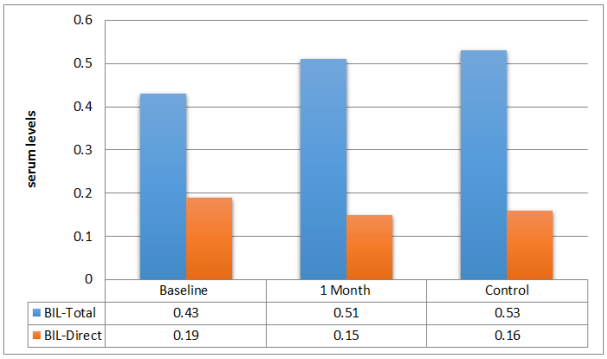

Fig-3: Demonstrate the serum levels of Bilirubin-Total and Bilirubin-Direct in diseased group at baseline and 1 month, and healthy control subjects

Table-5: Showed the correlation of clinical parameters versus to values of live function tests at baseline in diseased group

	PI		BI		PD		CAL	
	r	***P***	***r***	***P***	***r***	***P***	***r***	***P***
TP	0.089	0.751	-0.068	0.810	0.012	0.965	0.159	0.571
ALB	0.090	0.750	-0.106	0.706	-0.009	0.974	0.146	0.603
ALP	-0.124	0.659	-0.121	0.668	-0.009	0.975	-0.262	0.345
AST	-0.177	0.527	-0.059	0.833	-0.017	0.953	-0.091	0.748
ALT	0.324	0.239	0.229	0.411	0.308	0.263	0.079	0.779
BIL-D	-0.075	0.790	-0.339	0.217	0.025	0.929	0.375	0.168
BIL-T	-0.185	0.508	-0.073	0.795	0.004	0.988	0.111	0.693

Table-6: Showed the correlation of clinical parameters versus to values of live function tests at 1 month after periodontal therapy in diseased group

	PI		BI		PD		CAL	
	r	***P***	***r***	***P***	***r***	***P***	***r***	***P***
TP	0.192	0.492	0.223	0.423	-0.562*	0.029	-0.263	0.344
ALB	0.149	0.597	-0.162	0.565	-0.215	0.442	0.029	0.919
ALP	-0.347	0.205	0.004	0.989	-0.295	0.286	-0.172	0.540
AST	-0.221	0.428	0.178	0.525	-0.243	0.383	-0.237	0.396
ALT	0.248	0.373	-0.205	0.463	0.149	0.596	-0.147	0.601
BIL-D	-0.095	0.737	0.423	0.116	0.209	0.455	0.276	0.320
BIL-T	0.008	0.978	0.434	0.106	0.114	0.685	-0.008	0.978

DISCUSSION

The subgingival microbiota in patients with periodontitis provides a significant and persistent gram-negative bacterial challenge to the host that was met by a potent immunoinflammatory response [34]. These organisms and their products, such as lipopolysaccharide (LPSs), have ready access to the periodontal tissues and to the circulation via the sulcular epithelium, which is frequently ulcerated and discontinuous. The total surface area of pocket epithelium in contact with subgingival bacteria and their products in a patient with generalized moderate periodontitis has been estimated to be approximately the size of the palm of an adult hand, with even larger areas of exposure in cases of more advanced periodontal destruction [35]. Bacteremia to the periodontal tissues mount an immunoinflammatory response to bacteria and their products, systemic challenge with these agents also induces a major vascular response [5, 6, 13, 17]. Additionally, the host response may offer explanatory mechanisms for the interactions between periodontal infection and a variety of systemic disorders.

According to the previous hypothesis, the present study aimed to investigate the effect of periodontal therapy on the liver function tests, these purpose supported with some researches [21-24]. The non-surgical periodontal therapy of the moderate to severe chronic periodontitis patients revealed a significantly improvement in clinical parameters (PI, BI, PD and CAL). These findings agreed with several researches [21, 24, 36].

The serum levels of ALB were highly significantly decrease in CP patients compared to healthy individuals and significant increased after periodontal therapy. This outcome in consistent to Kaur *et al*., and Saravanan *et al.*, [37, 38], they suggested that decreasing of serum ALB concentration were associated with CP in comparison to healthy subjects. Moreover, the mean values of serum ALB were increased after periodontal treatment, this finding was supported with study of Shirmohammadi *et al*., [39], and they concluded that "decreases and increases in serum albumin levels under the effect of periodontal disease and its treatment indicated an inverse relationship between the albumin levels of serum and chronic periodontitis".

Serum TP total protein levels were high significant increase in CP patient at baseline in contrast to healthy subjects. These findings were parallel to research of Koregol *et al*., [40], they reported that the salivary TP may aid as an important biochemical indicator of chronic periodontitis. While the effect of periodontal therapy increased the levels of TP after 1 month, this result was matched to study of Rad *et al*., [41], they mentioned that gingival fluid levels of ALB, TP and globulin were significantly increased after treatment of periodontitis patients.

The diseased hepatic patient is characterized by decreasing the serum levels of ALB and TP [42]. For remark, the insignificant difference between the levels of ALB and TP at 1 month of periodontal treatment correspond to healthy subjects may reflect the beneficial effect of periodontal therapy to the liver health conditions. Total protein combined of ALB and globin [40, 41], more researches needed to investigate the levels of globin in relation to ALB in periodontitis patients before and after periodontal treatment.

The serum levels of ALT, AST were insignificant decreased after 1 month of periodontal therapy and baseline of CP patients versus to healthy. This observation notified the little effect of periodontal therapy and inconsistent with clinical study of Khatavkar *et al*., [24], they concluded that AST levels significantly decreased. While, the present study disagreement with previous study that mentioned no significant decreasing levels of ALT after periodontal treatment. Moreover, the levels of ALT and AST was insignificant increased in CP patients compared to healthy subjects, these outcomes dissimilarity with some studies [43, 44]. Furthermore, the insignificantly decreasing of ALT and AST after 1 month after periodontal therapy was adapted with a study of Hayashi *et al*., [45].

As regards to serum levels of ALP in current study, the statistical analysis shown no significant differences between baseline and 1 month after periodontal therapy. These notifications are contrary to Jeyasree *et al*., they concluded that serum ALP levels were significantly decreased following Phase I periodontal, therapy along with improvement in clinical parameters [46]. Serum levels of ALP in healthy subjects not significantly decreased in comparison to periodontitis patients, this finding was conflict to results of Soud *et al*., they reported that serum levels of ALP were significantly elevated in patients with chronic periodontitis and considered as a biomarker for periodontal disease [47].

Direct and indirect bilirubin levels are slightly decrease after periodontal therapy, this observation agree with findings of Ling *et al*., [48]. For amazing, the statistical comparison for levels of investigated tests at 1 month of periodontal therapy in contrast to healthy subjects showed no significance, these outcomes reflect the beneficial effectiveness of periodontal therapy.

The correlation of clinical periodontal parameters with investigated liver function test revealed only mild correlation of PD to levels of TP after treatment, this view in consent with results of some studies [40, 41]. For explanation, the insignificance correlation may refer to the study was performed on

systemic healthy patients. On the other hand, Mester *et al.*, [49] studied the periodontal parameters in-patients with liver fibrosis, they displayed an association between hepatic fibrosis and periodontal disease, patients with advanced liver fibrosis had higher values in clinical periodontal parameters.

For conclusions, the present study demonstrated the followings: (1) highly significant improvement of clinical parameters after periodontal therapy, (2) the examined liver function tests were decreased after periodontal therapy but not significant except significantly increasing the serum levels of TP and ALB. These results indicated that a beneficial effect of the periodontal therapy to diseased liver patients. More researches needed to clarify the effectiveness of periodontal therapy on large scale of healthy and diseased hepatic patients, and increased cooperation between dentists and physicians is strongly recommended.

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REFERENCES

1. Highfield J. Diagnosis and classification of periodontal disease. Australian dental journal. 2009 Sep;54:S11-26.
2. Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent Jr RL. Microbial complexes in subgingival plaque. Journal of clinical periodontology. 1998 Feb;25(2):134-44.
3. Borgnakke WS. The traveling oral microbiome. Chapter 4. In: Glick M, editor. The oral-systemic health connection: a guide to patient care. Chicago: Quintessence; 2014, 61-102.
4. Mealey BL, Klokkevold PR. Carranza's Clinical Periodontology, twelfth edition. Chapter 12. 2015, 202-213.
5. Han P, Sun D, Yang J. Interaction between periodontitis and liver diseases. Biomedical reports. 2016 Sep 1;5(3):267-276.
6. Grønkjær LL. Periodontal disease and liver cirrhosis: A systematic review. SAGE Open Medicine. 2015; 3(7):1-11.
7. Yoneda M, Naka S, Nakano K, Wada K, Endo H, Mawatari H, Imajo K, Nomura R, Hokamura K, Ono M, Murata S. Involvement of a periodontal pathogen, Porphyromonas gingivalis on the pathogenesis of non-alcoholic fatty liver disease. BMC gastroenterology. 2012 Dec;12(1):12-16.
8. Ahmad A, Furuta M, Shinagawa T, Takeuchi K, Takeshita T, Shimazaki Y, Yamashita Y. Association of periodontal status with liver abnormalities and metabolic syndrome. Journal of oral science. 2015;57(4):335-343.
9. Fernandez J, Gustot T. Management of bacterial infections in cirrhosis. Journal of hepatology. 2012 Jan 1;56:S1-S12.
10. Gustot T, Durand F, Lebrec D, Vincent JL, Moreau R. Severe sepsis in cirrhosis. Hepatology. 2009 Dec;50(6):2022-2033.
11. Fernández J, Navasa M, Gómez J, Colmenero J, Vila J, Arroyo V, Rodés J. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. Hepatology. 2002 Jan;35(1):140-148.
12. Fernández J, Acevedo J, Castro M, Garcia O, Rodríguez de Lope C, Roca D, Pavesi M, Sola E, Moreira L, Silva A, Seva-Pereira T. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: a prospective study. Hepatology. 2012 May;55(5):1551-1561.
13. Hyvärinen K, Tuomainen AM, Laitinen S, Bykov IL, Törmäkangas L, Lindros K, Käkelä R, Alfthan G, Salminen I, Jauhiainen M, Kovanen PT. Chlamydial and periodontal pathogens induce hepatic inflammation and fatty acid imbalance in apolipoprotein E-deficient mice. Infection and immunity. 2009 Aug 1;77(8):3442-3449.
14. Shapira L, Champagne C, Van Dyke TE, Amar S. Strain-Dependent Activation of Monocytes and Inflammatory Macrophages by Lipopolysaccharide ofPorphyromonas gingivalis. Infection and immunity. 1998 Jun 1;66(6):2736-2742.
15. Hirschfeld M, Weis JJ, Toshchakov V, Salkowski CA, Cody MJ, Ward DC, Qureshi N, Michalek SM, Vogel SN. Signaling by toll-like receptor 2 and 4 agonists results in differential gene expression in murine macrophages. Infection and immunity. 2001 Mar 1;69(3):1477-1482.
16. Ren J, Ding Y, Yu H, Zhou Y, Yu W. Effects on the expression of pro-inflammatory cytokines in the liver and spleen after oral administration of Porphyromonas gingivalis in mice. Biomedical Research. 2018;29(8):1603-1609.
17. Fialkow L, Wang Y, Downey GP. Reactive oxygen and nitrogen species as signaling molecules regulating neutrophil function. Free Radical Biology and Medicine. 2007 Jan 15;42(2):153-64.
18. Halliwell B. Free radicals, antioxidants, and human disease: curiosity, cause, or consequence?. The lancet. 1994 Sep 10;344(8924):721-4.
19. Tomofuji T, Ekuni D, Yamanaka R, Kusano H, Azuma T, Sanbe T, Tamaki N, Yamamoto T, Watanabe T, Miyauchi M, Takata T. Chronic administration of lipopolysaccharide and proteases induces periodontal inflammation and hepatic steatosis in rats. Journal of periodontology. 2007 Oct 1;78(10):1999-2006.
20. Sobaniec H, Sobaniec-Lotowska ME. Morphological examinations of hard tissues of paradontium and evaluation of selected processes of lipid peroxidation in blood serum of rats in the

course of experimental periodontitis. Medical Science Monitor. 2000;6(5):875-881.
21. Tomofuji T, Ekuni D, Sanbe T, Azuma T, Tamaki N, Irie K, Maruyama T, Yamamoto T, Watanabe T, Miyauchi M, Takata T. Effects of improvement in periodontal inflammation by toothbrushing on serum lipopolysaccharide concentration and liver injury in rats. Acta Odontologica Scandinavica. 2009 Jan 1;67(4):200-205.
22. Dos Santos Carvalho J, Cardoso Guimaraes Vasconcelos AC, Herlany Pereira Alves E, dos Santos Carvalho A, da Silva FR, de Carvalho Franca LF, de Padua Rocha Nobrega Neto A, Di Lenardo D, de Souza LK, Barbosa AD, Medeiros JV. Steatosis caused by experimental periodontitis is reversible after removal of ligature in rats. Journal of periodontal research. 2017 Oct;52(5):883-892.
23. Ni J, Chen L, Zhong S, Chai Q, Zhang L, Wang D, Li S, Zhang J. Influence of periodontitis and scaling and root planing on insulin resistance and hepatic CD36 in obese rats. Journal of periodontology. 2018 Apr;89(4):476-485.
24. Khatavkar PR. Effect of Scaling and Root Planing on Liver Function Test (Alanine Aminotransferase and Aspartate Aminotransferase) in Systemically Healthy–Chronic Periodontitis Subjects: A Clinical Trial. Dental Science, 2016; 3(10): 290-295.
25. Abrahamson JH, Terespolsky Y, Brook JG, Clark SL. Cornell Medical Index as a health measure in epidemiological studies. British journal of preventive and social medicine. 1965;19:103-110.
26. Ramfjord, SP, Emslie, RD, Greene, JC, Heldm AJ, Wear-Hauge J. Epidemiology studies of periodontal diseases, Am Journal Publ health. 1968; 58:1713-1722.
27. O'Leary, TJ, Drake, RB, Naylor, JE. The plaque control record. Journal of Periodontology. 1972;43(1): 38-38.
28. Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. International Dental Journal, 1975;4(25): 229-235.
29. Dumas BT, Watson AH, Biggs HG. Albumin standards and the measurement of serum albumin with bromcrescol green. Clinica Chimica Acta. 1997;258(1): 21-30.
30. Lubran MM. The measurement of total serum proteins by the Biuret method. Ann Clin Lab Sci. 1978; 8(2):106-110.
31. Garber CC. Jendrassik--Grof analysis for total and direct bilirubin in serum with a centrifugal analyzer. Clin Chem. 1981;27(8): 1410-1416.
32. Huang XJ, Choi YK, Hyung-Soon, Yarimaga OK, Yoon E, Kim HS. Aspartate aminotransferase (AST/GOT) and alanine Aminotransferase (ALT/GPT) detection techniques. Sensors (Basel). 2006;6(7): 756-782.
33. Babson AL, S J Greeley SJ, Coleman CM, Phillips GE. Phenolphthalein monophosphate as a substrate for serum alkaline phosphate. Clinical Chemistry. 1966; 12(8): 482-90.
34. Offenbacher S, Barros SP, Beck JD. Rethinking periodontal inflammation. Journal of periodontology. 2008 Aug;79:1577-1584.
35. Page RC. The pathobiology of periodontal diseases may affect systemic diseases: inversion of a paradigm. Annals of periodontology. 1998 Jul 1;3(1):108-20.
36. Bresolin AC, Pronsatti MM, Pasqualotto LN, Nassar PO, Jorge AS, da Silva EA, Nassar CA. Effectiveness of periodontal treatment on the improvement of inflammatory markers in children. Archives of oral biology. 2014 Jun 1;59(6):639-644.
37. Kaur N, Kaur N, Sarangal V. A study to evaluate the correlation of serum albumin levels with chronic periodontitis. Indian Journal Dent Res. 2015;26(1): 11-4.
38. Saravanan AV, Swaminathan RM, Panishankar KH, Kumar P. Estimation of serum albumin levels associated with chronic periodontitis in elderly subjects - A cross sectional study. SRM University Journal of Dental Sciences. 2012, 3(2):120-126.
39. Shirmohammadi A, Faramarzi M, Salari A, Shamami MS, Babaloo AR, Mousavi Z. Effect of non-surgical periodontal treatment on serum albumin levels in patients with chronic periodontitis. Journal of Periodontology & Implant Dentistry. 2018 Jan 1;10(1):18-23.
40. Koregol AC, More SP, Korego SC, Nagaraj KN. Total protein in gingival crevicular fluid as indicators of periodontal disease activity: A clinico biochemical analysis. Drug Development and Therapeutics. 2015, 6(1):15-19.
41. Rad AB, Saghafi S, Hashemi E, Aghasizadeh E, Ebrahimi F, Banihashem A, Rajaei S. Comparison of albumin, total protein, globulin and enzyme activity Creatine Phospho Kinase (CPK) in the Gingival Crevicular Fluid of patients with chronic periodontitis before and after treatment. Int. J. of Multidisciplinary and Current research. 2018 Sep; (6):1091-1096.
42. Clementine YF, Tar CA. Liver function tests (LFTs). Proceedings of singapore healthcare. 2010, 19(1):80-83.
43. Patil PB, Patil B. Estimation of gingival crevicular fluid aspartate aminotransferase levels in periodontal health and disease. Journal of the International Clinical Dental Research Organization. 2011 May 1;3(2):64-76.
44. Siddique S, Panchmal GS, Pullishery F. Aspartate Aminotransferase as a biomarker in periodontal disease: A comparative in vitro study. Saudi Journal of Oral Sciences. 2016 Jan 1;3(1):21-24.
45. Hayashi J, Hasegawa A, Hayashi K, Suzuki T, Ishii M, Otsuka H, Yatabe K, Goto S, Tatsumi J, Shin K. Effects of periodontal treatment on the medical status of patients with type 2 diabetes

mellitus: a pilot study. BMC oral health. 2017 Dec;17(1):77.

46. Jeyasree R, Theyagarajan R, Sekhar V, Navakumar M, Mani E, Chendilmaran et al. Evaluation of serum and salivary alkaline phosphatase levels in chronic periodontitis patients before and after nonsurgical periodontal therapy. J Indian Soc Periodontol. 2018 Nov-Dec; 22(6): 487–491.
47. Soud P, Gupta H, Kumar P, Sethi S, Chandra A, Yadav N. Estimation and Comparison of Levels of Alkaline Phosphatase (ALP), Acid Phosphatase (ACP), Calcium (Ca) and Potassium (K) in Serum of Subjects with and Without Periodontal Disease (PD). International Journal of Applied Dental Sciences. 2015; 1(4): 90-93.
48. Xu JL, Meng HX, Li Z, Li FY, Zhang L. Effect of periodontal therapy on metabolic control and serum biochemical markers in subjects with type 2 diabetes and chronic periodontitis. Journal of Peking University (Health Science). 2013; Feb 18;45(1):27-32.
49. Mester A, Lucaciu O, Ciobanu L, Apostu D, Buhatel D, Campian R. Assessments of periodontal parameters in patients with liver fibrosis according to Metavir score. International Journal of the Bioflux Society. 2018; 10(2):42-45.