



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS



15 MAR 2017

MEMORANDUM FOR SGDTT
ATTN: CAPT SARAH M RINGDAHL

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **The Relationship between Fatty Liver Disease and Periodontal Disease** presented at/published to **American Academy of Dental Research (AADR) San Francisco, CA, 22 March 2017** in accordance with MDWI 41-108, has been approved and assigned local file #**17144**.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
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LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

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The Relationship Between Fatty Liver Disease and Periodontal Disease



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ABSTRACT

Periodontitis is a highly prevalent and destructive chronic disease. Numerous studies support an association between periodontal disease and other systemic diseases (diabetes, cardiovascular disease, chronic kidney disease, adverse pregnancy outcome, etc). Non-alcoholic fatty liver disease (NAFLD) is a chronic inflammatory disease that is characterized by accumulation of triglycerides and fat in the liver which may lead to fibrosis and even cirrhosis. The mechanism of this destruction is due to activation of inflammatory cells and upregulation of cytokines, much like the chronic inflammatory destruction seen in periodontal disease. The association between these two diseases has never been investigated. A reasonable mechanism in which periodontal disease may play a role in the destruction seen in NAFLD is the remote site infection of periodontal disease. Chewing and oral hygiene measures lead to systemic release of bacterial byproducts and subsequent systemic inflammatory response which may subsequently lead to the changes seen in the liver. **Objective:** The purpose of this cross-sectional study is to investigate the relationship between periodontal disease and NAFLD.

MATERIALS and METHODS

Liver diagnosis and blood draw: Patients with a diagnosis of NAFLD determined from previous liver biopsy were recruited for this study. Patients were seen at the hepatology clinic for informed consents and blood draw for cytokine panel and liver enzyme assay (including aspartate aminotransferase (AST) and alanine aminotransferase (ALT)). Patients were subsequently scheduled at the dental clinic for periodontal examination. Liver diagnoses were categorized based on severity of cirrhosis with stage 1 and 2 having no cirrhosis and stage 3 and 4 having cirrhosis.

Periodontal examination: Full mouth periodontal examinations were completed by a single examiner (S.R.) who remained blinded to liver diagnosis until after data entry. A UNC-15 probe was used to measure probing depths (PD) and clinical attachment level (CAL) on 6 sites/tooth. Sites with bleeding were also recorded at 6 sites/tooth. Plaque index was measured at 4 sites/tooth following use of disclosing agent. Third molars were excluded from examination. Severity of periodontal disease was defined as mean PD and mean CAL. Extent of PD was determined by the percentage of sites having ≥ 3 mm CAL and percentage of sites having PD of 5mm or greater. Periodontal diagnosis was made using the CDC-AAP periodontal disease criteria as mild (defined as ≥ 2 interproximal sites having ≥ 3 mm CAL and ≥ 2 interproximal sites with PD >3 mm not on the same tooth, or ≥ 1 site with ≥ 5 mm PD), moderate (defined as ≥ 2 interproximal sites having ≥ 4 mm CAL or ≥ 2 interproximal sites with PD ≥ 5 mm not on the same tooth), or severe (defined as ≥ 2 interproximal sites having ≥ 6 mm CAL and ≥ 1 interproximal site with PD ≥ 5 mm).

Exclusion criteria: Patients with less than 12 teeth, co-existing autoimmune disorders, currently taking antibiotics, or pregnant/breast feeding women were excluded from the study. Additionally, patients who did not take recommended antibiotic prophylaxis were excluded. Patients were not excluded for having diabetes or for current tobacco use.

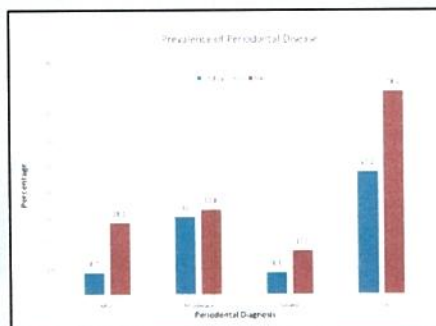
Statistical Analysis: Demographic data was analyzed using mean values and ranges. Statistical analyses were made using Spearman Rank correlation. Significance was defined by a $p < 0.05$.

RESULTS

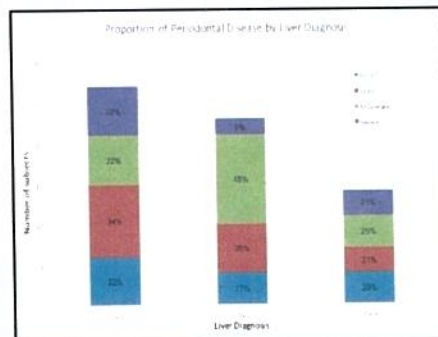
A total of 64 patients have completed the liver biopsy and periodontal exam portions of this research project and were included in data analysis. The mean age for included patients was 56 years (range 32-79). Male patients comprised 67% of our population. The average number of teeth per patient was 25.45 (range 15-28).

None of the patients included in this study were current smokers, however, 28% were former smokers. Average BMI was 33.3 (range 24-44.3). 54% of the subjects had diagnosis of type II diabetes mellitus.

Of the patients completing study protocol (a total of 64) 78% of included patients had some degree of periodontal disease, with 28% having mild, 33% having moderate, and 17% having severe periodontal disease (See graph below.)



When evaluating the breakdown of periodontal disease severity by liver diagnosis, in the group with fatty liver disease without cirrhosis (LDx1), 78% had some degree of periodontal disease, with 34% being mild, 22% moderate, and 22% having severe periodontal disease. In the patients with mild liver cirrhosis, 83% had some degree of periodontal disease, with 26% having mild, 48% having moderate, and 9% having severe disease. In the group of patients with more extreme liver cirrhosis, 71% had some form of periodontal disease with 21% having mild, 29% having moderate, and 21% having severe disease (see graph below).



The Spearman rank correlation coefficient reached significance when comparing AST and ALT values to the periodontal diagnosis [AST: -0.33 ($p=0.02$) and ALT: -0.43 ($p=0.002$)] and the presence or absence of periodontal disease [AST: -0.28 ($p=0.047$) and ALT: -0.34 ($p=0.01$)]. ALT values were also inversely related to the percentage of sites with ≥ 3 mm CAL [-0.29 ($p=0.04$)].

The statistical analysis of the liver diagnosis to the various periodontal disease measures of extent and severity (percentage of sites with PD ≥ 5 mm, percentage of sites with CAL ≥ 3 mm, mean PD, mean CAL, bleeding index, and plaque index), found none of the correlation coefficients to be significant.

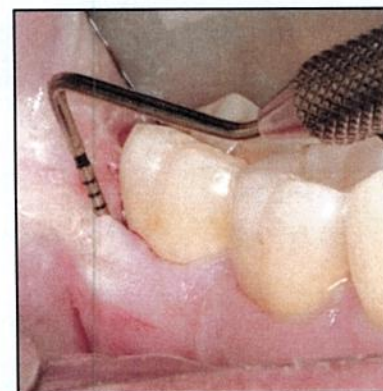
DISCUSSION

In a preliminary data analysis of this cross-sectional study evaluating the relationship between periodontal disease and non-alcoholic fatty liver disease, there was no statistical relationship between severity of NAFLD and periodontal disease severity or extent.

A statistically significant inverse relationship between periodontal disease diagnosis and AST and ALT values was seen. A significant inverse relationship with ALT value and percentage of sites with ≥ 3 mm CAL was also seen.

Although our number of subjects is too small to draw conclusions in regard to prevalence, there appears to be a larger proportion of periodontal disease in this population of patients with NAFLD than in the general US population.

Continued research will focus on increasing number of subjects and analyzing specific inflammatory cytokine values (IL-1, IL-6, IL-8, TNF- α , CRP), CD4:CD8 ratio and presence or absence of CMV antibodies to the severity of periodontal disease and NAFLD.



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