802

# Relationship between Gingival Inflammation and Systemic Bio-Markers: Impact of Smoking and Systemic Anti-Oxidants

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## ABSTRACT

Periodontitis, smoking and blood levels of anti-oxidants have been related to various systemic diseases. **Objective:** Correlate clinical measures of periodontal disease and blood levels of bio-markers in a cross-sectional survey of adults and compare those correlations within subsets of the population. **Methods:** Enrolled subjects (n=505, 74.7% female, mean age=44.6, 61.1% non-smokers) assessed for whole mouth Löe-Silness Gingival Index (GI) and pocket depth (PD) (overall mean GI=1.1 and mean PD=2.2 mm). Blood samples collected and analyzed for whole blood and serum bio-markers. Relationships between biomarkers and clinical measures computed using a Pearson correlation. **Results:** For the overall group GI was negatively correlated (p<0.01) with serum Apo-lipoprotein A-1 (Apo A-1) and folate (Fol) (r=-0.29 and -0.24) and positively correlated (p<0.05) with hematocrit (Hc), Hemoglobin (Hb), and WBC counts (r=0.15, 0.14, and 0.17). PD correlated with Apo A1, Fol, Hc and Hb (r=-0.29, -0.17, 0.19, and 0.18). Smokers had markedly more correlations than non-smokers. Smokers GI correlated with Apo A-1, Fol, Hb, Hc and WBC (r=-0. 41, -0.43, 0.22, 0.22, 0.25). Non-smokers GI only correlated with Apo A-1 (r=-0.22)]. Similar differences between smokers and non-smokers were seen for correlations with PD. Since smoking is related to decreased blood anti-oxidants, subject subsets with serum vitamin E or C above (Hi) or below (Lo) the median values were compared for correlations. GI for Lo E subjects' correlated (p<0.05 and r>0.2) with 7 systemic bio-markers (e.g. Apo-lipoprotein B: r=0.3), GI for Hi E subjects' correlated with 1 bio-marker (not Apo-B). Differences for Hi/Lo C subjects were less dramatic. **Conclusions: Adult GI and PD correlate with systemic bio-marker levels, smokers have more correlates than non-smokers, and Lo E subjects' bio-markers have more correlates with GI than Hi E subjects. Together these findings suggest smoking and systemic anti-oxidant levels may impact on the relationship of gingival inflammation with systemic bio-markers.**

## INTRODUCTION

Clinical measures of periodontitis have been related to peripheral blood bio-marker levels and risk factors for atherosclerosis. Smoking and reduced serum anti-oxidant levels have been related to periodontal measures and implicated as risk factors for atherosclerosis. Smoking alters blood anti-oxidant levels. Smoking has been considered as a possible confounder in the proposed etiologic relationship between periodontitis and atherosclerosis.

## OBJECTIVE

Determine if gingivitis and pocket depth are correlated to systemic bio-markers in a normal adult population. Determine whether smoking and/or serum anti-oxidant levels impact on the relationships between the periodontal measures and systemic bio-markers.

## MATERIALS AND METHODS

- Blood samples obtained from 417 adults.
  - 300 females, 117 males; mean age = 44.6 (21 to 91 yrs); 61.1% non-smokers
  - Fasting blood collected on 226 subjects to analyze for Apolipoproteins A-1 and B
- Clinical measures:

| | |
|---|---|
| • Löe-Silness Gingival Index (GI) assessed at six sites/tooth:<br>• Pocket depth (PD) assessed at six sites/tooth: | Overall mean =1.1<br>Overall mean = 2.2 mm |

- Blood samples analyzed for:
  - Whole blood: Hemoglobin, Hematocrit, WBC count, Basophils, RBC count, Neutrophils, Monocytes, Platelets
  - Serum: Apo-lipoprotein A-1, Apo-lipoprotein B, C-reactive protein (CRP), fibrinogen, folate, alpha-tocopherol (Vit E), ascorbate (Vit C), and uric acid.
- Pearson correlations calculated for bio-markers and clinical measures for overall group and indicated subgroups.
- Linear regression modeling done for interaction of quartiles of systemic Vit E and C with relationship between measures of periodontal disease and systemic bio-markers.

## RESULTS

### Correlation of GI and Gingival Bleeding with Systemic Bio-markers: Effects of Smoking

| Systemic Bio-Markers | Total Panel | Non Smokers | Past or Current Smokers |
|---|---|---|---|
| Apolipoprotein A - 1 | -0.29 (-0.27) | -0.22 (-0.21) | -0.41 (-0.36) |
| Apolipoprotein B | | 0.26 (0.20) | |
| Folic Acid, Serum | -0.24 (-0.25) | | -0.43 (0.40) |
| Hb | 0.14 (0.12) | | 0.23 (0.19) |
| HCT | 0.15 (0.13) | | 0.22 (0.17) |
| RBC Count | 0.22 (0.21) | 0.22 (0.24) | 0.23 (0.20) |
| WBC Count | 0.16 (0.16) | | 0.22 (0.15) |
| Neutrophils | 0.16 (0.15) | | 0.24 (0.18) |

* Pearson correlations significant @ p< 0.05; in most cases p<0.01.
( ) = Correlations for gingival bleeding; GI=2
- Current/past smokers have more correlates than non-smokers

### Correlation of PD with Systemic Biomarkers: Effect of Smoking

| Systemic Bio-Markers | Total Panel | Non Smokers | Past or Current Smokers |
|---|---|---|---|
| Apolipoprotein A - 1 | -0.294 | -0.216 | -0.371 |
| Folic Acid, Serum | -0.172 | | -0.255 |
| Uric Acid | 0.182 | 0.155 | 0.186 |
| Hb | 0.184 | | 0.287 |
| HCT | 0.197 | | 0.299 |
| RBC Count | 0.213 | 0.178 | 0.258 |
| Monocytes | 0.188 | 0.138 | 0.198 |

* Pearson Correlations significant @ p< 0.05; in most cases p<0.01.
- Current/past smokers have more correlates than non-smokers

*Research presented at the 80th General Session of the IADR, March 6-9, 2002*

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802

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Pg. 2

## Correlation of GI and Gingival Bleeding with Systemic Bio-Markers: Effect of Systemic Anti-Oxidant Levels

| Systemic Bio-Markers | Low Vit C** | High Vit C** | Low Vit E** | High Vit E** |
|---|---|---|---|---|
| Apolipoprotein A -1 | -0.23 | -0.29 (-0.31) | -0.20 | -0.34 (0.33) |
| Apolipoprotein B | 0.24 | | 0.30 (0.28) | |
| CRP | | | | |
| Folic Acid, Serum | -0.19 (0.20) | -0.206 (0.24) | -0.20 (-0.18) | -0.17 (0.22) |
| Uric Acid | | | 0.16 (0.18) | |
| Hb | | | 0.22 (0.22) | |
| HCT | | 0.14 (0.15) | 0.22 (0.22) | |
| RBC Count | 0.24 (0.22) | | 0.28 (0.27) | |
| WBC Count | (0.22) | | 0.22 (0.20) | |
| Neutrophils | 0.20 (0.23) | | 0.19 (0.18) | |
| Monocytes | | | 0.18 (0.19) | |

* Pearson correlations significant @ $p < 0.05$ ; in most cases $p < 0.01$.
( ) = correlates for gingival bleeding
** Subject subsets defined by above/below serum median value of Vit E and C
- Low serum Vit E subjects have more correlates than high Vit E subjects.

## Correlation of PD with Systemic Bio-Markers: Effect of Systemic Anti-Oxidant Levels

| Systemic Bio-Markers | Low Vit C | High Vit C | Low Vit E | High Vit E | Lo Vit E + Lo Vit C** | Hi Vit E + Hi Vit C** |
|---|---|---|---|---|---|---|
| Apolipoprotein A -1 | -0.32 | 0.26 | -0.26 | -0.30 | -0.37 | -0.29 |
| Apolipoprotein B | | | 0.20 | | | |
| Folic Acid, Serum | | -0.20 | -0.19 | -0.14 | 0.18 | -0.24 |
| Uric Acid | | 0.20 | 0.19 | 0.18 | 0.18 | |
| Hb | | 0.19 | | 0.24 | 0.18 | |
| HCT | | 0.22 | 0.15 | 0.25 | 0.16 | 0.20 |
| Platelets | | -0.16 | | | | |
| RBC Count | | -0.18 | 0.22 | 0.21 | 0.23 | |
| WBC Count | 0.16 | | | | | |
| Neutrophils | 0.15 | | | | | |
| Monocytes | 0.20 | 0.17 | 0.16 | 0.21 | | |

* Pearson correlations significant @ $p < 0.05$ ; in most cases $p < 0.01$.
** Subsets include subsets above/below serum medians for both Vit E and C.
-Directionally more correlates amongst subjects low in both Vit's E & C, but also in high C subjects.

## Serum Vitamins C and E: Interactions* with Correlates between Gingival Parameters and Systemic Bio-markers

| Systemic Bio-Markers | Vit E with GI | Vit E with GI=2 | Vit E with PD | Vit C with GI | Vit C with GI=2 | Vit C with PD |
|---|---|---|---|---|---|---|
| Apolipoprotein A -1 | 0.008 | | | | | |
| Apolipoprotein B | | 0.02 | 0.004 | | | |
| CRP | 0.04 | | | | | 0.04 |
| Fibrinogen | 0.01 | | | | | |
| Uric Acid | | 0.03 | | | | |
| Hb | | 0.03 | | | | |
| HCT | | 0.02 | | | | |
| RBC Count | | 0.01 | | | | |
| Platelets | | | | 0.004 | 0.003 | |
| WBC Count | | | | | 0.001 | |
| Neutrophils | | | | 0.05 | 0.002 | |
| Basophils | | | 0.007 | | | |
| Eosinophils | | | 0.05 | | | |

* Linear regression analyses for significant interactions (p values indicated) of quartiles of systemic Vit E and C with the indicated correlates.
-Serum levels of Vit E and C interact with the correlates between blood bio-markers (and cell types) and measures of gingival bleeding, gingivitis and pocket depth.

## CONCLUSION

Gingivitis, gingival bleeding, and pocket depth are correlated to systemic levels of a series of peripheral blood bio-markers and cell types in a broad based population.

Smoking and decreased serum levels of vitamin E (and to some degree decreased Vit C) increase the number of correlations for levels of gingivitis (and gingival bleeding) with serum bio-markers and peripheral blood cells.

These findings suggest smoking and serum anti-oxidant levels may impact on the mechanistic interaction of gingivitis and periodontal disease with blood cell types and bio-markers and may define subpopulations of subjects for whom these interactions are stronger.

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