ABSTRACT

Background: Oxidative stress and inflammatory responses can arise from similar exposures, and are interrelated at the cellular level through NF-κB. Experimental stressors can activate both systems of response.
Objective: To explore the presence and magnitude of paired associations between diagnostic biomarkers of oxidation and inflammation from the same or different anatomical compartments.
Methods: 82 children, 38 girls and 44 boys (median age 56 mo), attending 3 daycare centers from a government-subsidized system in Quetzaltenango, Guatemala, delivered single samples of urine, whole blood, saliva, and feces for one or more of the selected determinations. We were able to make pairing correlations of Among 23 biomarker variables, paired Spearman rank-order correlations could be made from 12 from the inflammatory domain (White blood cells , plasmatic and salivary IL-1β, IL-6, IL-8, IL-10 and TNFα, and fecal calprotectin) and 11 from the oxidation domain (urinary markers of oxidation {15-Isoprostane-F2t and 8-hydroxy-deoxy-guanosine}; erythrocyte activity of antioxidant enzymes {catalase , superoxide dismutase , glutathione reductase and glutathione peroxidase}; and plasmatic concentrations of antioxidant nutrients {retinol, tocopherols, β-carotene and Coenzymes Co-Q9 and Co-Q10}). The SPSS version 20 software program was used.
Results: Within the 132-cell full matrix, 13 statistically-significant associations were found (9.8% of possible), seven at a p-value of <0.01 and 6 from <0.05 to 0.01. Superoxide dismutase and β-carotene were each associated with 5 and 6 inflammatory biomarkers, respectively. Backward-elimination multiple-regression analyses with both as dependent variables showed the same two predictors, plasmatic TNF-α and saliary IL-8, with an r2-value of 0.155 for superoxide dismutase and r2 0.136 for β-carotene.
Conclusion: Significant associations in an inter-class context between paired, oxidation-vs-inflammation biomarker variables represent only a 10th of the possible associations and a fraction of the 33-57% association seen with the same data, previously analyzed on an intra-class hemi-matrix basis.

SCANT INTERACTIONS OF BIOMARKERS OF OXIDATIVE STRESS AND ANTI-OXIDATION DEFENSE WITH THOSE OF THE INFLAMMATORY RESPONSE AMONG PRESCHOOL CHILDREN FORM THE WESTERN HIGHLANDS OF GUATEMALA

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BACKGROUND

All organisms are constantly subjected to external (environmental, dietary) or endogenous (metabolic, pathological) influences that can incite an inflammatory response in the immune system[1] or an excess generation of oxidative free radicals[2].

What the associations would be for biomarkers of the respective classes of stress/response in free-living humans is minimally explored.

OBJECTIVE

To explore the presence and magnitude of paired associations between diagnostic biomarkers of oxidation and inflammation from the same or different anatomical compartments.

METHODS

Setting: Three government-subsidized daycare centers in a semi-urban (center A), a marginal-urban (center B) and a rural (center C) settings of Quetzaltenango, in the Western Highlands of Guatemala.

Subjects: A total of 82 preschool children, 38 girls and 44 boys (median age 56 months), enrolled in the study.

Sample collection: We spent 8 weeks at each daycare center to observe the delivery of the 40-day rotating menu of the Secretariat of the Beneficial Works of the First Lady System (*SOSEP*), and during the last 3 weeks of the process, each child delivered single samples of blood, 24-h urine, feces and saliva.

Study variables: A total of 23 biomarker variables from whole blood, plasma, saliva, urine and feces were measured, distributed as follows: 11 from an oxidation/anti-oxidation domain [F2-Isoprostane (F2-Iso) and 8-hydroxydeoxyguanose (8-OHdG) in urine; activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPX) and glutathione reductase (GSR) in red blood cells; and circulating retinol, β-carotene, tocopherol, and coenzymes Co-Q9 and Co-Q10] and 12 from the inflammatory domain [white blood cells (WBC), fecal calprotectin and IL-1β, IL-6, IL-8 and TNF-α in both plasma and saliva].

Ethical considerations: The Human Subjects Committee of CeSSIAM granted the study protocol ethical approbation, written consent form was signed by a parent or guardian. This study was registered at clinicaltrials.gov as NCT02203890.

Data analysis: Spearman rank-order correlation coefficient, and goodness-of-fit models were performed in order to determine associations between variables of the two domains using the IBM, SPSS version 20 software.

RESULTS

Figure1 : Characteristics of the samples disaggregated by setting and sex.

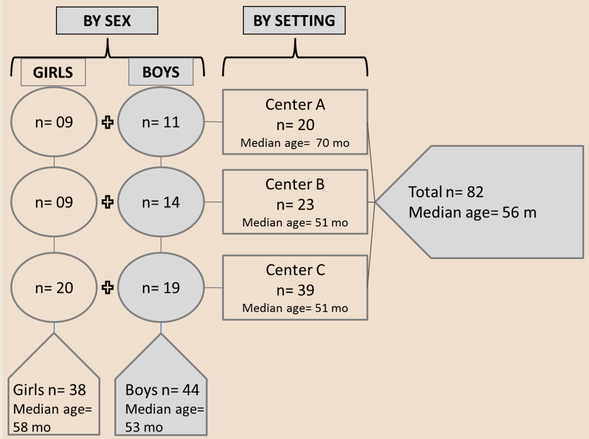
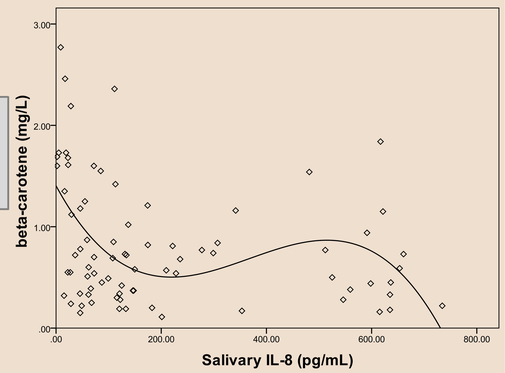


Figure 2: Association between β-carotene and salivary IL-8 with the superimposition of the Goodness-of-fit cubic curve form (r=0.452).



- By pair-wise Spearman rank-order correlation coefficient analysis involving a 132-cell matrix, 13 statistically-significant associations (9.8%) were found, seven at a p value of <0.01.
- Goodness-of-fit models enhanced the strength of association in 11 instances. SOD and β-carotene were each associated with five and six inflammatory biomarkers, respectively (Table).
- Backward-elimination multiple-regression analyses with both as dependent variables showed the same two predictors, plasmatic TNF-α and salivary IL-8, with an r-value of 0.394 for SOD and 0.368 for β-carotene (data not shown)

Table: Comparison of Spearman and non-linear correlations coefficients in inter-biomarkers significant associations with ascending order by Spearman values.

			Goodness-of-fit r-value	Curve form	Goodness-of-fit r-value	Curve form
Oxidation variable	**Inflammation variable**	**Spearman rank-order r-value**	**Oxidation as Independent (x-axis) variable**		**Inflammation as Independent (x-axis) variable**	
SOD	Plasmatic IL-1β (n=82)	-0.239	0.217	Sigmoid	0.292*	Cubic
	Plasmatic IL-8 (n=82)	0.277	0.276	Cubic	0.280	Cubic
	Plasmatic TNF-α (n=82)	0.294	0.335*	Quadratic	0.334*	Power
	Salivary IL-8 (n=80)	0.263	0.360*	Power	0.409*	Sigmoid
	Salivary TNF-α (n=80)	0.262	0.216	Power	0.254	Cubic
Retinol	Calprotectin (n=81)	-0.227	0.170	Exponential	0.211	Cubic
	Plasmatic IL-6 (n=81)	-0.226	0.268*	Cubic	0.249*	Power
β-carotene	WBC (n=81)	-0.322	0.292	Cubic	0.250	Cubic
	Plasmatic IL-10 (n=81)	-0.288	0.270	Power	0.286	Sigmoid
	Plasmatic TNF-α (n=81)	-0.363	0.342	Power	0.348	Sigmoid
	Salivary IL-8 (n=79)	-0.310	0.432*	Exponential	0.452*	Cubic
	Salivary IL-10 (n=79)	-0.290	0.317*	Exponential	0.427*	Inverse
	Salivary TNF-α (n=79)	-0.307	0.227	Exponential	0.248	Cubic

*Improvement on the r-value using the oxidation or inflammation variable as independent (x) axis on the appropriate curve form.

DISCUSSION/CONCLUSION

Both oxidative and inflammatory stress biomarkers show wide variation – but relative elevation – in low-income and deprived preschoolers of predominantly Mayan ascent sharing a highly uniform dietary offering.

As compared to our previous work with interactions among the bi-omarkers within the domains of oxidation[3] or of inflammation[4], the find-ings here are nowhere as robust or harmonic when examined **across** the two domains.

Beta-carotene and SOD, on the oxidation side, and salivary IL-8 and IL -10 and plasmatic TNF-α, on the inflammation side, stand out for the consistency in their associations.

Finally, the salivary cytokines have the great advantage in children of their non-invasive collection procedure

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