Evaluation of serum prestin as a new potential biomarker for hearing damage due to lead exposure in population from Tlaxcala, Mexico

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Key points

- Divalent metals have been classified as ototoxicants[4].
- Lead has been considered as potential ototoxic from the inner ear.
- Prestin protein is expressed ~~only~~ in outside hairy cells from the inner ear[3].
- Serum prestin levels change due to noise and ototoxic drugs[1].
- At the time there is no biomarker for hearing impairment, and only 1% of the population have access to get an audiometry test[2].
- Hearing damage reduce hearing response affecting social behavior.
- The aim of this study was to evaluate serum prestin and the relation with hearing damage in participants exposed to environmental and occupational lead.

Methods

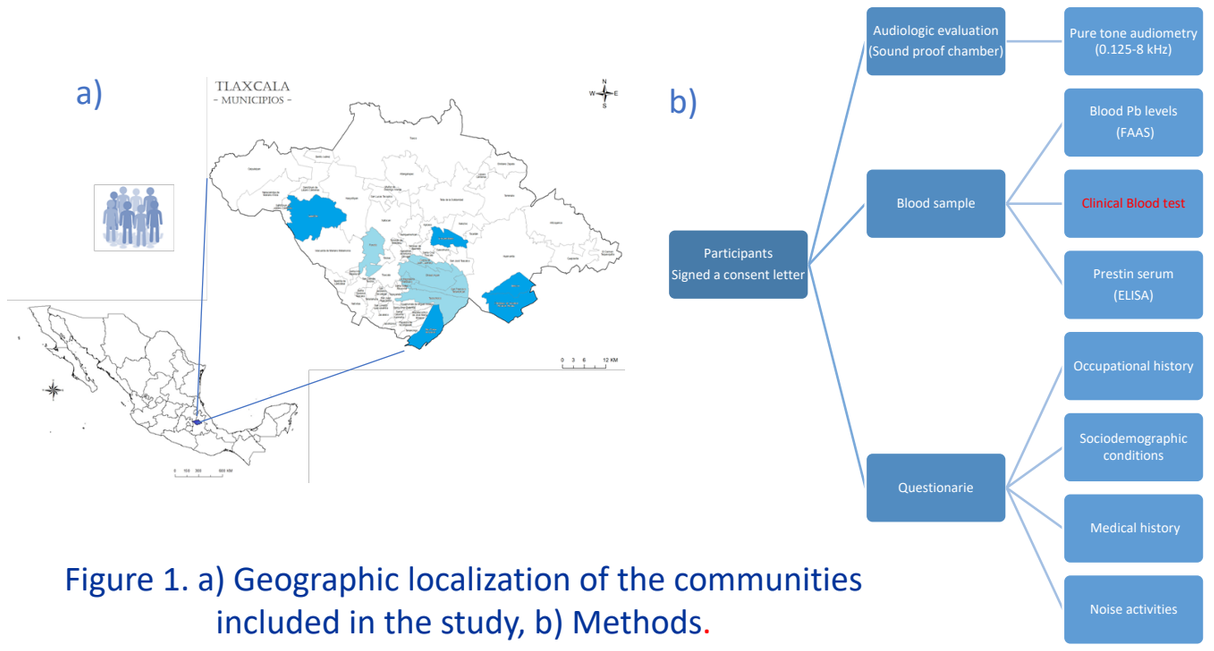

Figure 1. a) Geographic localization of the communities included in the study, b) Methods.

RESULTS

I. General characteristics and exposure risk for hearing loss

Table 1. General characteristics of the study population according to lead exposure

	All n=315	Group I n=111	Group II n=204	p-value
***Male**, n(%)*	147 (47%)	45 (41%)	102 (50%)	0.068
***Female**, n(%)*	168 (53%)	66 (59%)	102 (50%)	
***Age** years, M(IQR)*	42 (34-52)	43 (34-53)	42 (34-51)	0.499
***Age** ≤39 years, n(%)*	130 (41%)	31 (25-36)	31 (24-36)	0.471
***Age** ≥40 years, n(%)*	185 (59%)	50.5 (44-58)	49 [43-55]	
***BMI** Kg/m², M(IQR)*	27.9 (25.3-31.1)	28.2 (25.2-31.8)	27.9 (25.3-30.5)	0.458
***BMI** normal, n(%)*	74 (23%)	26 (23%)	48 (24%)	0.550
***BMI** overweight-obesity, n(%)*	241 (77%)	85 (77%)	156 (76%)	
***SBP** mmHg, M(IQR)*	119 (111.6-129)	118.6 (110.6-126)	120.6 (112.3-129.3)	0.075
***DBP** mmHg, M(IQR)*	71.6 (65.6-77)	70.8 (65.3-70.8)	72 (66-77)	0.364
***Normal BP**, n(%)*	284 (90%)	97 (87%)	187 (92%)	0.154
***High BP**, n(%)*	31 (10%)	14 (13%)	17 (8%)	
***Glycaemia** mg/dl, M (IQR)*	96 (90-105)	95 (90-103)	97 (90-107)	0.386
***Normal glycaemia**, n(%)*	281 (89%)	101 (91%)	180 (88%)	0.291
***High glycaemia**, n(%)*	34 (11%)	10 (9%)	24 (12%)	
***Triglycerides** mg/dl, M (IQR)*	156 (116-219)	167 (123-236)	150 (109.5-209)	0.083
***Normal triglycerides**, n(%)*	147 (47%)	46 (41%)	101 (49%)	0.105
***High triglycerides**, n(%)*	168 (53%)	65 (59%)	103 (50%)	
***c-HDL** mg/dl, M (IQR)*	42.6 (36-51)	43 (35-51)	42 (37-51)	0.944
***Low c-HDL**, n(%)*	178 (56%)	62 (56%)	116 (57%)	0.478
***High c-HDL**, n(%)*	137 (44%)	49 (44%)	88 (43%)	
***c-LDL** mg/dl, M (IQR)*	114 (93-133)	114 (94-137)	114 (93-133)	0.982
***Low c-LDL**, n(%)*	108 (34%)	39 (35%)	69 (34%)	0.455
***High c-LDL**, n(%)*	211 (66%)	72 (65%)	135 (66%)	
***Tcol** mg/dl, M (IQR)*	180 (155-205)	183 (154-207)	179 (155-204.5)	0.569
***Low Tcol**, n(%)*	268 (85%)	91 (82%)	177 (87%)	0.165
***High Tcol**, n(%)*	47 (15%)	20 (18%)	27 (13%)	
***MS risk**[a], n(%)*	239 (76%)	88 (79%)	151 (74%)	0.183
***No MS risk**[a], n(%)*	76 (24%)	23 (21%)	53 (26%)	

M: median, IQR: interquartile range, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, BP: blood pressure c-HDL: high density lipoprotein cholesterol, c-LDL: low density lipoprotein cholesterol, Tcol: total cholesterol, MS: metabolic syndrome. BMI: normal <25 kg/m², overweight or obesity ≥25 kg/m². BP: normal ≤129/80 mmHg, high ≥130/85 mmHg. Glycaemia: normal <126 mg/dl, high ≥126 mg/dl. Triglycerides: normal <150 mg/dl, high ≥150 mg/dl. c-HDL: low <40 mg/dl, high >40 mg/dl. c-LDL: low <100 mg/dl, high >100mg/dl. Total cholesterol: low <200 mg/dl, high >200 mg/dl.
[a]MS risk: presence of two or more risk factors for metabolic syndrome (high triglycerides, hypertension, low c-HDL, high blood glucose, high hip-waist index).

Table 2. Hearing loss risks factors and blood lead levels of the study population

	All n=315	Group I n=111	Group II n=204	p-value
***BPb** µg/dl, M (IQR)*	14 (7.5-22.6)	6 (3.9-7.7)	20.7 (14.6-28.4)	<0.001
***Women BPb** µg/dl, M (IQR)*	12.5 (6.6-20.8)	5.7 (3.8-7.5)	17.7 (13.6-25.5)	<0.001
***Men BPb** µg/dl, M (IQR)*	16.9 (8.3-25.8)	6.5 (4.2-8)	21.8 (16.2-36.8)	<0.001
***LGC user**, n(%)*	295 (94%)	100 (90%)	195 (96%)	0.050
***LGC worker**, n(%)*	207 (68%)	52 (47%)	155 (79%)	<0.001
***Noise activities per month**[a], n(%)*	194 (62%)	75 (67%)	119 (59%)	0.068
***Earphones use**, (n%)*	80 (25%)	33 (30%)	47 (23%)	0.122
***Smoking**, n(%)*	83 (26%)	33 (30%)	50 (25%)	0.192

BPb: blood lead level, M: median, IQR: interquartile range, LGC: lead-glazed ceramics.
[a]Record for one or two noise activities per month (motorcycle, hair dryer, firearms use).

II. Auditory function

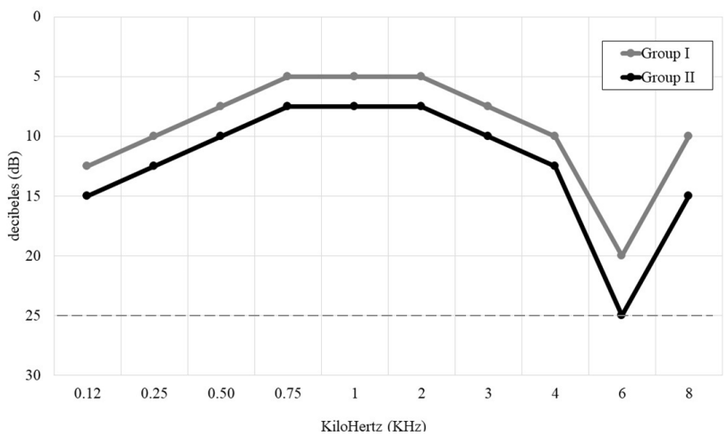

Figure 2. Pure tone audiometry for best ear (median value) according to blood lead levels (dash line indicate normal hearing threshold

III. Serum prestin levels

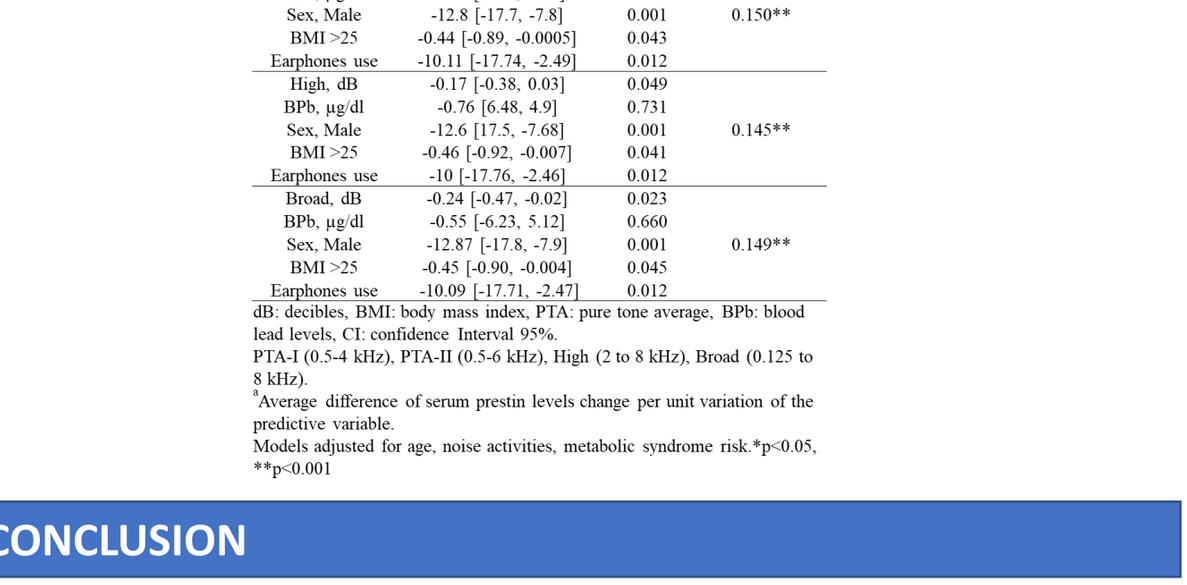

Figure 3. a) serum prestin levels, b) scaterploot and correlation for serum prestin levels according to PTA- value according to BPb groups (n=253), Rho -0.12, p=0.045.

IV. Robust multiple linear regression models

Table 4. Robust multiple linear regression model to prestin serum levels (ng/mL) of the study population

Predictive variables	β-Coeficient [CI 95%][a]	p-value	R^2 (n=253)
Pta-I, dB	-0.26 [-0.46,-0.06]	0.007	
BPb, µg/dl	-0.49 [-6.1, 5.1)	0.629	
Sex, Male	-12.8 [-17.8, -7.9]	0.001	0.151**
BMI >25	-0.4 [-0.8, 0.009]	0.049	
Earphones use	-10.14 [-17.77, -2.51]	0.011	
Pta-II, dB	-0.25 [-0.47, -0.03]	0.002	
BPb, µg/dl	-0.50 [-6.18, 5.18]	0.073	
Sex, Male	-12.8 [-17.7, -7.8]	0.001	0.150**
BMI >25	-0.44 [-0.89, -0.0005]	0.043	
Earphones use	-10.11 [-17.74, -2.49]	0.012	
High, dB	-0.17 [-0.38, 0.03]	0.049	
BPb, µg/dl	-0.76 [6.48, 4.9]	0.731	
Sex, Male	-12.6 [17.5, -7.68]	0.001	0.145**
BMI >25	-0.46 [-0.92, -0.007]	0.041	
Earphones use	-10 [-17.76, -2.46]	0.012	
Broad, dB	-0.24 [-0.47, -0.02]	0.023	
BPb, µg/dl	-0.55 [-6.23, 5.12]	0.660	
Sex, Male	-12.87 [-17.8, -7.9]	0.001	0.149**
BMI >25	-0.45 [-0.90, -0.004]	0.045	
Earphones use	-10.09 [-17.71, -2.47]	0.012	

dB: decibles, BMI: body mass index, PTA: pure tone average, BPb: blood lead levels, CI: confidence Interval 95%.
PTA-I (0.5-4 kHz), PTA-II (0.5-6 kHz), High (2 to 8 kHz), Broad (0.125 to 8 kHz).
[a]Average difference of serum prestin levels change per unit variation of the predictive variable.
Models adjusted for age, noise activities, metabolic syndrome risk.*p<0.05, **p<0.001

CONCLUSION

Our data indicate that lead exposure is related to an increase in hearing threshold, and serum prestin protein decreased according to the hearing threshold increase. This is the first study to evaluate prestin as a potential biomarker for hearing damage due to lead exposure without noise exposure. Also, this study showed important differences between prestin concentration in women and men.

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REFERENCES

[1]Parham 2014,[2]Cheatham 2015, [3]Dogan 2018, [4]Roth 2016