



ADRENAL DYSREGULATION IN CHILDREN WHO WERE BORN EXTREMELY PREMATURE: A PILOT STUDY.

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Introduction

The prevalence of hypertension in children and adolescent who were extremely preterm newborns (EP; ≤ 32 gestational weeks) has been found to be higher than in those born at term. The causes have not been well characterized. Studies support that adrenal dysregulation might be a consequence of prematurity.

Objective

To investigate if children who were extremely preterm newborns (≤ 32 gestational weeks) had higher adrenal hormones and vascular remodeling biomarker than term newborn (≥ 38 gestational weeks).

Subjects & Methods

- Setting: School of Medicine, Pontificia Universidad Católica de Chile.
- Design: A pilot cross-sectional study.
- Children (n=235, range 5,1-15,5 years old) from the community were invited to participate; 12 were EP (5%) with a gestational age between 30 and 32 weeks, and 223 were born at term with a gestational age between 38 and 40 weeks.
- Aldosterone, plasma renin activity (PRA), cortisol and cortisone were measured. Aldosterone/PRA ratio and cortisol/cortisone ratio were calculated. Matrix metalloproteinase-2 (MMP-2) activity evaluated by zymography was used as a vascular remodelling biomarker and their results were expressed in arbitrary units (calculated as the number of changes relative to the reference plasma used as an internal control). The results were expressed as median, p25th and p75th. They were analysed using nonparametric testing.

Results

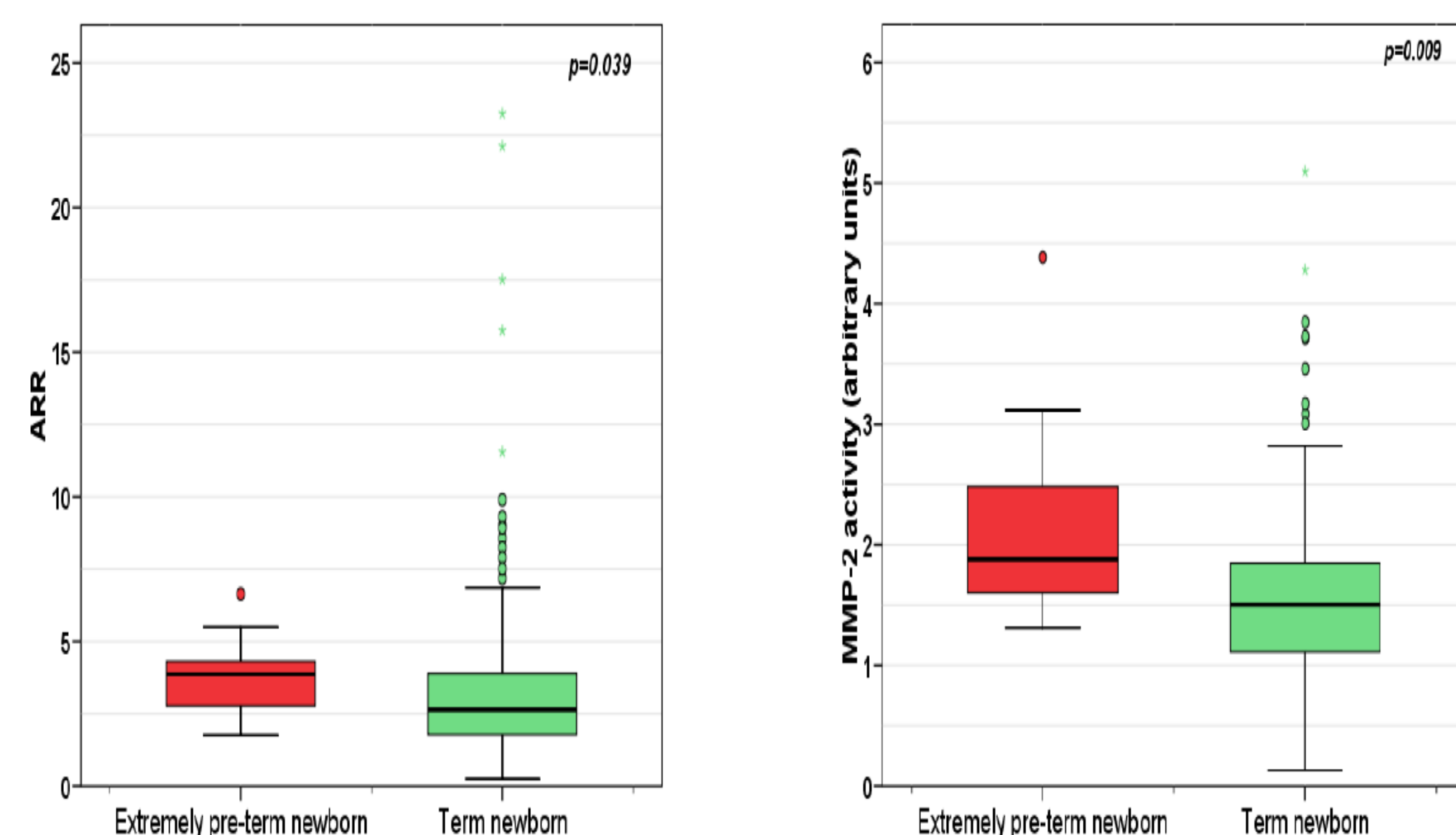
Table 1.- Clinical characteristics of the subjects distributed by gestational age

	Extremely pre-term newborns (n=12)			Term newborns (n=223)			p
	Median	p25 th	p75 th	Median	P25 th	p75 th	
- Age (years)	10.2	7.9	10.8	11.7	9.4	13.3	0.075
- Height (SDS)	0.48	-0.10	1.28	0.23	-0.35	0.90	0.434
- BMI (SDS)	1.13	0.54	1.38	1.20	0.21	1.73	0.434
- Body fat (%)	21	14	31	26	17	36	0.142
- Abdominal perimeter (cm)	71	67	75	74	64	85	0.346
- SBP index	1.09	1.04	1.17	1.06	1.00	1.13	0.184
- DBP index	1.11	1.06	1.18	1.11	1.01	1.19	0.797
Neonatal characteristics							
- Gestational age (weeks)	30	30	32	39	38	40	<0.001
- Birth length (SDS)	0.25	-0.75	0.50	0.25	-0.50	1.00	0.296
- Birth weight (SDS)	0.06	-0.83	1.08	0.22	-0.39	0.91	0.627

SDS: standard deviation score, SBP index: systolic blood pressure index, DBP index: diastolic blood pressure index.

At the time of this study, both groups were comparables in age, height-SDS, BMI-SDS, body fat, abdominal perimeter and blood pressure corrected by gender, age and height. Moreover no differences were observed in birth length and weight standard deviation score.

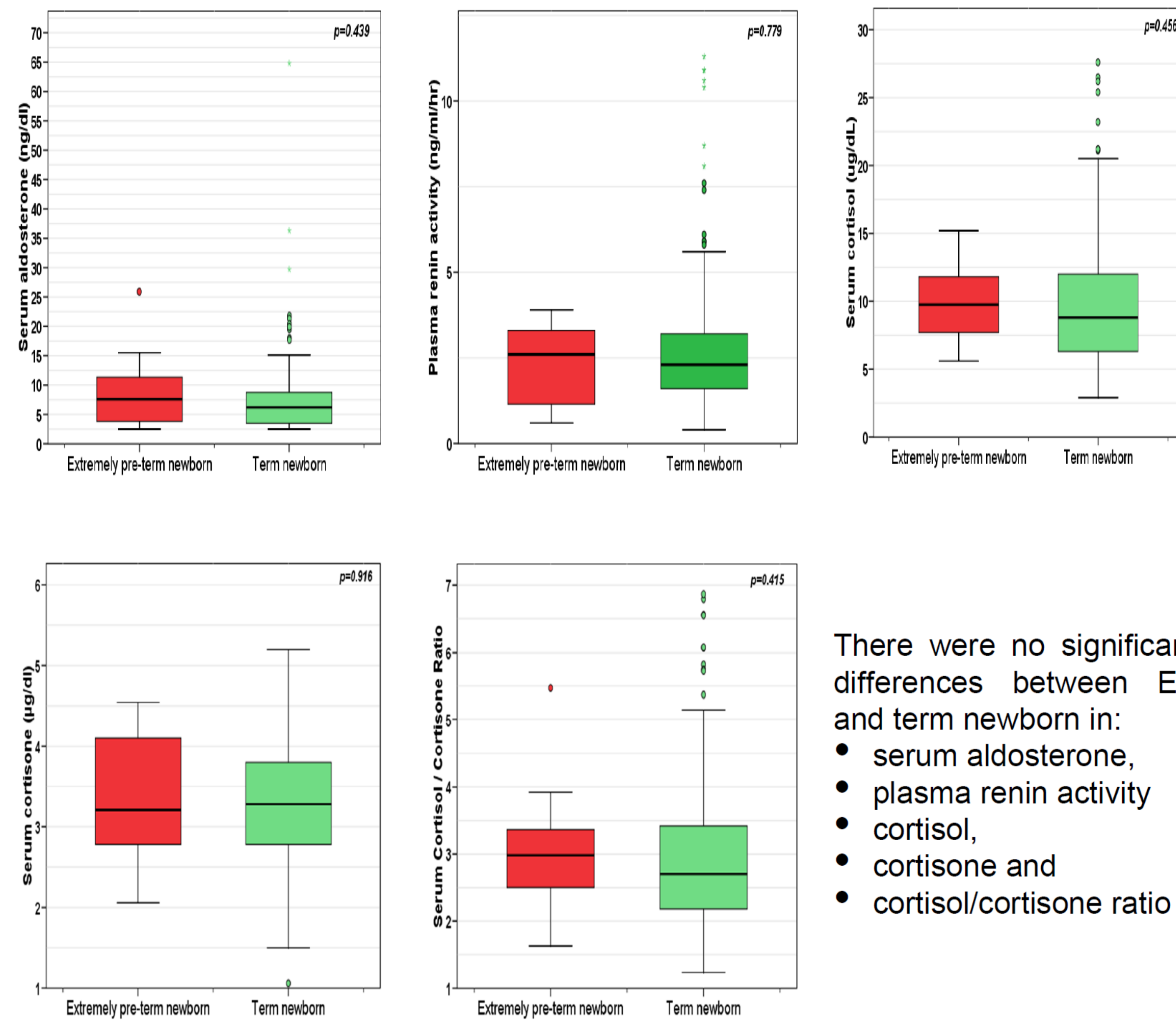
Figure 2.- Aldosterone/PRA ratio and MMP-2 activity in extremely pre-term newborns and term newborns.



Children who were born EP versus term newborns showed:

- higher aldosterone / PRA (ARR; 3.9 [2.8-4.3] vs. 2.6 [1.8-3.9], P=0.039) and
- higher MMP-2 activity (1.88 [1.60-2.48] vs. 1.50 [1.11-1.85] arbitrary units, P=0.009)

Figure 1.- Aldosterone, PRA, cortisol, cortisone and cortisol/cortisone ratio values in extremely pre-term newborns and term newborns.



There were no significant differences between EP and term newborn in:

- serum aldosterone,
- plasma renin activity
- cortisol,
- cortisone and
- cortisol/cortisone ratio

Conclusion

This pilot study showed that children who were extremely preterm newborns have higher ARR and vascular remodeling than children born at term, despite similar blood pressure. Future studies to assess the importance of these findings in early prevention of hypertension are warranted.

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