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Oxidative stress biomarkers relate to arterial stiffness and blood pressure in 6–8-year-old boys stratified by maternal risk: The ASOS study

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Background

- Higher CVD risk in families with hypercholesterolaemia [1,2].
- Use of confirmed family history of CVD was described a significant cardiovascular risk factor [3–5].
- CVD has a long asymptomatic period of development [6], starting as early as the first decade of life [7].
- Early identification of cardiovascular compromise in children is important to implement prevention and early treatment strategies [8].

Objectives

1. We aimed to compare blood pressure and arterial stiffness along with oxidative stress-related markers in black and white South African boys (6–8 years old) stratified by maternal risk predetermined from self-reported cardiovascular disease and lifestyle risk factors.
2. We investigated the links of blood pressure and arterial stiffness with oxidative stress-related markers in these groups.

Study sample and methods

Study sample

- Included 40 black and 41 white boys between 6 and 8 years old, along with the biological mother of each child (for stratification purposes).
- Ethical clearance number: NWU-00007-15-A1

Measurements included:

- Pulse wave velocity (PWV) was measured (Complior SP Acquisition System) at various sites and corrected for 80% distance travelled (also corrected for mean arterial pressure in all statistical analyses)
- Blood pressures were recorded (Omron HEM-759-E (705 IT) device (Omron Healthcare, Tokoyo, Japan)
- Urine samples were collected for analyses of thiobarbituric acid reactive substances (**TBARS**), 8-hydroxy-2-deoxy guanosine (**8-OHdG**), albumin and creatinine, as well as **uACR**

Statistical analysis

- All statistical analyses were performed using **IBM® SPSS® version 23** (IBM Corporation, Armonk, NY).
- We used **G*Power 3.1.9.2** to compute our required sample sizes for exploring these questions in a group of 6 to 8-year old boys.

Group stratification

- In **Microsoft Excel 2013**, the risk of the mother was calculated from the questionnaire data using the VLOOKUP function.
- Each subject was appointed a household number.
- The young study population were then stratified according to the appropriate self-reported CVD and/or lifestyle risk column of the mother.
- The formula used matched the household number of the children with that of the parent.
  - Coding=0; if the mother did not present with any CVD and/or lifestyle risk
  - Coding=1; if the mother presented with CVD and/or lifestyle risk

Table 1. General characteristics of boys stratified by maternal cardiovascular and/or lifestyle risk.

	Nonmaternal risk (n = 26)	Maternal risk (n = 55)	p Value
Age (months)	90.5 ± 10.6	93.7 ± 8.9	.19
Ethnicity, n (Black) (%)	8 (30.8)	33 (60)	.018
Body composition			
Body mass index (kg/m^2)	16.5 ± 2.0	16.1 ± 1.9	.36
Height (cm)	125.3 ± 7.4	126.2 ± 6.4	.26
Waist circumference (cm)	57.4 ± 6.3	57.6 ± 5.5	.27
Cardiovascular profile			
Blood pressure measurements			
Systolic blood pressure (mmHg)	105 ± 10	104 ± 9	.45
Diastolic blood pressure (mmHg)	69 ± 9	65 ± 9	.74
Pulse pressure (mmHg)	36 ± 8	39 ± 7	.63
Total peripheral resistance (mmHg/ml/s)	3.23 ± 1.48	3.03 ± 1.49	.85
Arterial stiffness indices			
Systemic arterial stiffness			
Arterial compliance (ml/mmHg)	0.802 ± 0.708	0.918 ± 0.756	.37
Regional arterial stiffness			
Carotid radial pulse wave velocity (m/s)[a]	9.55 ± 1.57	8.67 ± 2.01	.26
Carotid femoral pulse wave velocity (m/s)[a]	5.00 ± 0.86	4.68 ± 0.84	.052
Carotid dorsalis pedis pulse wave velocity (m/s)[a]	5.36 ± 0.65	5.19 ± 0.68	.50
Biochemical analyses			
Urinary albumin to creatinine ratio (mg/mmol)	0.914 ± 0.727	1.28 ± 0.65	.038
Thiobarbituric acid-reactive substances (ng/g creatinine)	6.51 ± 4.65	6.62 ± 3.97	.31
8-Hydroxy-2-deoxy Guanosine (ng/g creatinine)	124.8 ± 75.5	132.4 ± 74.9	.93

Values are arithmetic mean ± standard deviation or geometric mean (5th and 95th percentiles).

[a]PWV was adjusted for mean arterial pressure.

Table 3. Partial correlation analyses of cardiovascular and biochemical variables with TBARS and 8-OHdG of boys stratified according to maternal cardiovascular and/or lifestyle risk.

	TBARS (ng/g creatinine)		
	Nonmaternal risk ($n = 26$)	Maternal risk ($n = 55$)	Total group ($n = 81$)
Systolic blood pressure (mmHg)	$r = -0.097$; $p = .659$	$r = 0.110$; $p = .439$	$r = 0.052$; $p = .649$
Diastolic blood pressure (mmHg)	$r = 0.190$; $p = .386$	$r = 0.274$; $p = .050$	$r = 0.205$; $p = .072$
Pulse pressure (mmHg)	$r = -0.326$; $p = .129$	$r = -0.165$; $p = .243$	$r = -0.165$; $p = .148$
Arterial compliance (ml/mmHg)	$r = -0.006$; $p = .979$	$r = 0.163$; $p = .247$	$r = 0.155$; $p = .176$
Total peripheral resistance (mmHg/ml/s)	$r = -0.026$; $p = .908$	$r = -0.174$; $p = .218$	$r = -0.140$; $p = .223$
Mean arterial pressure (mm/Hg)	$r = 0.212$; $p = .331$	$r = -0.092$; $p = .518$	$r = -0.044$; $p = .701$
Carotid radial pulse wave velocity (m/s)[a]	$r = 0.494$; $p = .019$	$r = 0.091$; $p = .524$	$r = 0.272$; $p = .017$
Carotid femoral pulse wave velocity (m/s)[a]	$r = 0.174$; $p = .438$	$r = 0.292$; $p = .038$	$r = 0.293$; $p = .010$
Carotid dorsalis pedis pulse wave velocity (m/s)[a]	$r = 0.241$; $p = .280$	$r = 0.513$; $p < .001$	$r = 0.474$; $p < .001$
Urinary albumin to creatinine ratio (mg/mmol)	$r = -0.466$; $p = .025$	$r = -0.281$; $p = .046$	$r = -0.426$; $p < .001$

Adjusted for age, body mass index, and ethnicity.
[a]PWV was additionally adjusted for mean arterial pressure.
n: number of participants; TBARS: thiobarbituric acid-reactive substances; 8-OHdG: 8-hydroxy-2-deoxy guanosine.

Table 3. Partial correlation analyses of cardiovascular and biochemical variables with TBARS and 8-OHdG of boys stratified according to maternal cardiovascular and/or lifestyle risk.

	8-OHdG (ng/g creatinine)		
	Nonmaternal risk ($n = 26$)	Maternal risk ($n = 55$)	Total group ($n = 81$)
Systolic blood pressure (mmHg)	$r = -0.410$; $p = .052$	$r = 0.145$; $p = .310$	$r = 0.064$; $p = .583$
Diastolic blood pressure (mmHg)	$r = -0.117$; $p = .596$	$r = 0.288$; $p = .040$	$r = 0.165$; $p = .152$
Pulse pressure (mmHg)	$r = -0.310$; $p = .150$	$r = -0.136$; $p = .342$	$r = -0.105$; $p = .362$
Arterial compliance (ml/mmHg)	$r = -0.008$; $p = .973$	$r = 0.116$; $p = .418$	$r = 0.109$; $p = .346$
Total peripheral resistance (mmHg/ml/s)	$r = 0.104$; $p = .636$	$r = 0.088$; $p = .538$	$r = 0.069$; $p = .551$
Mean arterial pressure (mm/Hg)	$r = -0.084$; $p = .703$	$r = 0.364$; $p = .009$	$r = 0.312$; $p = .006$
Carotid radial pulse wave velocity (m/s)[a]	$r = -0.345$; $p = .116$	$r = 0.068$; $p = .640$	$r = -0.030$; $p = .800$
Carotid femoral pulse wave velocity (m/s)[a]	$r = -0.535$; $p = .010$	$r = 0.095$; $p = .512$	$r = -0.093$; $p = .426$
Carotid dorsalis pedis pulse wave velocity (m/s)[a]	$r = 0.022$; $p = .921$	$r = 0.191$; $p = .185$	$r = 0.128$; $p = .272$
Urinary albumin to creatinine ratio (mg/mmol)	$r = 0.429$; $p = .041$	$r = 0.310$; $p = .027$	$r = 0.330$; $p = .003$

Adjusted for age, body mass index, and ethnicity.
[a]PWV was additionally adjusted for mean arterial pressure.
n: number of participants; TBARS: thiobarbituric acid-reactive substances; 8-OHdG: 8-hydroxy-2-deoxy guanosine.

Table 4. Multiple regression analyses of cardiovascular and biochemical variables with oxidative stress markers of boys stratified in the maternal cardiovascular/lifestyle risk group only.

	Thiobarbituric acid-reactive substances (ng/g creatinine)			
	Adj R^2	B (95%CI)	β	p Value
Maternal risk group (n = *55)*				
Diastolic blood pressure (mmHg)	0.159	0.173 (0.000; 0.273)	0.293	.050
Carotid femoral pulse wave velocity (m/s)[a]	0.158	1.41 (0.083; 2.737)	0.297	.038
Carotid dorsalis pedis pulse wave velocity (m/s)[a]	0.322	2.97 (1.545; 4.398)	0.505	<.001
Urinary albumin to creatinine ratio (mg/mmol)	0.161	−4.16 (−8.22; −0.086)	−0.261	.046
	8-Hydroxy-2-deoxy guanosine (ng/g creatinine)			
Diastolic blood pressure (mmHg)	0.273	2.54 (0.120; 4.96)	0.289	.040
Carotid femoral pulse wave velocity (m/s)[a]	0.304	7.56 (−15.44; 30.56)	0.084	.512
Carotid dorsalis pedis pulse wave velocity (m/s)[a]	0.323	18.18 (−8.99; 45.35)	0.164	.185
Urinary albumin to creatinine ratio (mg/mmol)	0.283	80.54 (9.521; 151.55)	0.268	.027

Covariates included in this model: age, body mass index and ethnicity.
[a]PWV was additionally adjusted for mean arterial pressure.
n: number of participants.

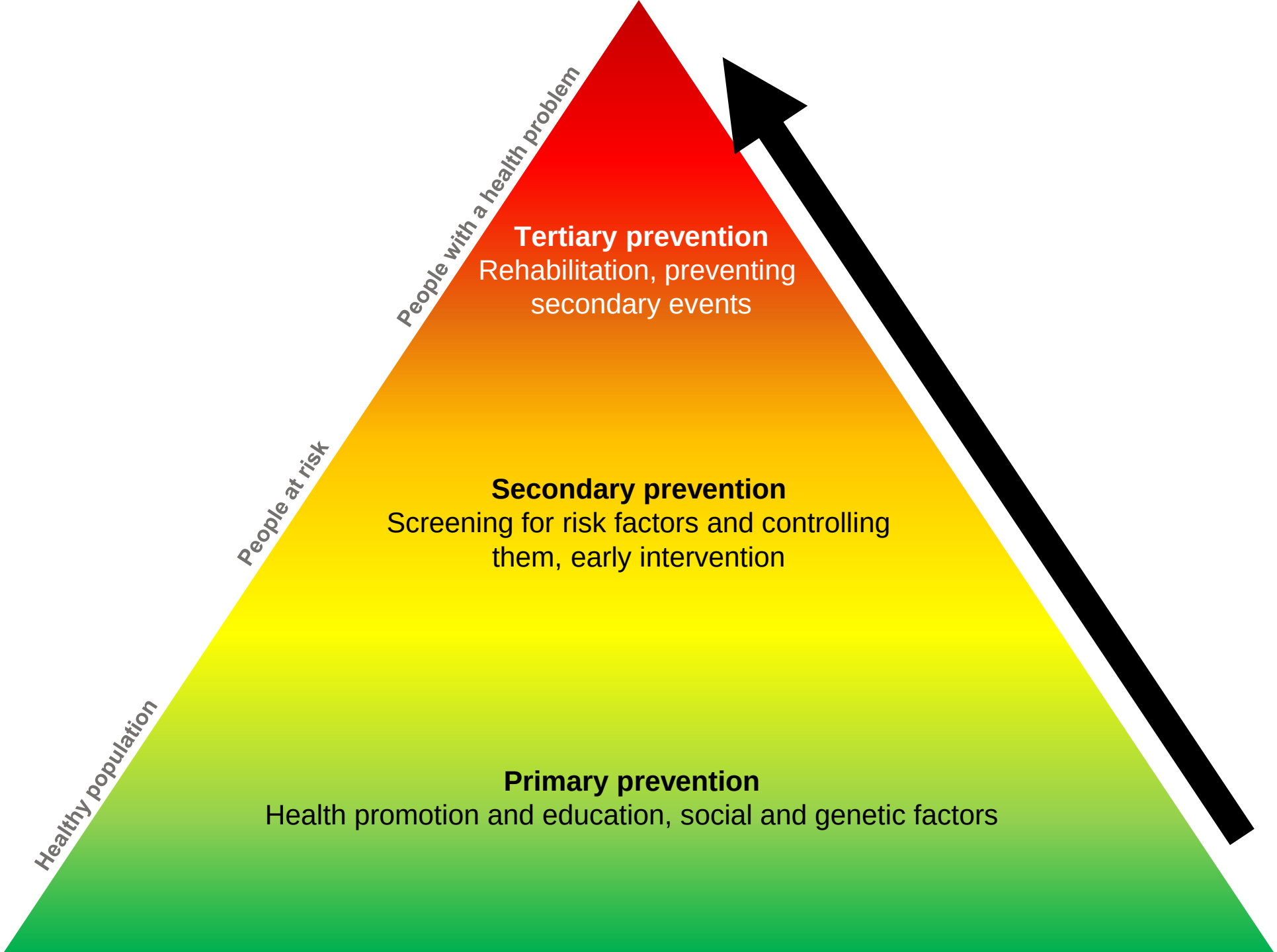
Discussion

- **Systolic vs diastolic blood pressure**
  - **SBP** remain a strong predictor of cardiovascular mortality in middle-aged to elderly individuals [9].
  - **DBP** indicates cardiovascular risk in children as the pulse wave is reflected during diastole, resulting in an elevated mean diastolic blood pressure affecting the cardiac afterload [10].

- Our results may hint to the potential early onset of endothelial dysfunction.
  - Apart from uACR being a reliable marker of renal function it was also reported as an early marker of endothelial dysfunction in youth [11].

- A large part of lifestyle determinants, often seen in the general population:
  - physical inactivity-associated obesity;
  - cigarette smoke, and
  - high alcohol consumption

all lead to an increase in ROS making the vasculature susceptible to the harmful effects of oxidative stress [12].


People with a health problem
People at risk
Healthy population
Tertiary prevention
Rehabilitation, preventing secondary events
Secondary prevention
Screening for risk factors and controlling them, early intervention
Primary prevention
Health promotion and education, social and genetic factors

Conclusion

- In children as young as 6 years of age, oxidative stress related to arterial stiffness, diastolic blood pressure and urinary ACR.

- This association was only evident in children with linked maternal lifestyle and cardiovascular risk factors.

- Our results indicate **oxidative stress as an early mediator of vascular compromise** in 6–to–8-year-old young male participants with family linked cardiovascular and lifestyle risk.

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