

Birthweight and its association with retinal vessel equivalents – Results from the population-based German Gutenberg Health Study

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Low birthweight (BW) is associated with arterial hypertension in adulthood. However, the pathophysiological mechanism is still unclear, and BW-related vascular alterations may be important intermediate steps. In a previous report, authors observed that foetal growth restriction leads to an adverse microvascular development in young adults (Hellstrom et al. 2004). Consequently, vascular alterations of former low birthweight newborns may be a mechanism leading to an increased risk for hypertension. Hence, this study aims to assess the retinal vessel characteristics and their correlation with foetal growth restriction indicated by self-reported birthweight in a large German population-based cohort.

The Gutenberg Health Study (GHS) is a prospective, population-based, observational cohort study. Fundus photographs of participants aged 35 to 74 years were analysed using the

'retinal vessel analyser' software (IME-DOS, Jena, Germany) measuring the central retinal arteriolar equivalent (CRAE) and the central retinal venular equivalent (CRVE). BW was self-reported. The association between BW and retinal vessel metrics was analysed using uni- and multivariable linear regression analyses with adjustment for potential confounders which were reported to be associated with retinal vessel metrics (age, sex, spherical equivalent, mean arterial blood pressure).

In a GHS subsample of participants with self-reported birthweight, retinal vessel metrics were successfully assessed in 2476 participants (1338 female, aged 51.9 ± 10.5 years). CRAE was descriptively $3.6 \mu\text{m}$ smaller in the low birthweight group compared to the normal birthweight group. In univariate analysis, CRAE showed no association with birthweight (model #1: $B = 0.03 [-0.08; 0.14] \mu\text{m}$ per 100 g; $p = 0.59$; $R^2 = 0.0001$). When adjusting for age, sex and spherical equivalent, CRAE was smaller in adults with low birthweight (model #2: $B = 0.10 [0.00; 0.20] \mu\text{m}$ per 100 g; $p = 0.042$), but this effect was weakened when additional adjusting for mean arterial blood pressure (model #3: $B = 0.08 [-0.01; 0.17] \mu\text{m}$ per 100 g; $p = 0.09$) (Table 1). No association was observed between low birthweight and CRVE, neither in univariate nor in multivariable analyses.

Our study provides new investigations on the association of birthweight and retinal vessel morphology. Our

Table 1. Associations of central retinal arteriolar and venular equivalent with birthweight in the Gutenberg Health Study (2007–2012)

	Model 1		Model 2		Model 3	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
<i>Central retinal arteriolar equivalent (μm)</i>						
Birthweight (per 100g)	0.03 (–0.08; 0.14)	0.59	0.10 (0.00; 0.20)	0.042	0.08 (–0.01; 0.17)	0.089
Age [years]			–2.92 (–3.23; –2.61)	<0.001	–2.29 (–2.59; –1.99)	<0.001
Sex [female]			5.21 (3.96; 6.46)	<0.001	3.07 (1.87; 4.28)	<0.001
Spherical equivalent [dioptrre]			3.35 (3.10; 3.61)	<0.001	3.35 (3.11; 3.60)	<0.001
MAP [mmHg]					–0.45 (–0.51; –0.40)	<0.001
<i>Central retinal venular equivalent (μm)</i>						
Birthweight (per 100g)	0.00 (–0.11; 0.10)	0.95	–0.02 (–0.11; 0.08)	0.71	–0.02 (–0.12; 0.07)	0.67
Age [years]			–1.47 (–1.77; –1.17)	<0.001	–1.43 (–1.74; –1.12)	<0.001
Sex [female]			1.64 (0.40; 2.87)	0.009	1.46 (0.20; 2.72)	0.024
Spherical equivalent [dioptrre]			3.60 (3.35; 3.86)	<0.001	3.60 (3.34; 3.86)	<0.001
MAP [mmHg]					–0.03 (–0.08; 0.03)	0.35

CI = confidence interval; g = gram; MAP = mean arterial blood pressure.

Linear regression models were performed assessing the association of central retinal vessel equivalents with birthweight (continuous).

Model 1: univariate; model 2: adjusted for age (years), sex (female), spherical equivalent (dioptrre); model 3 adjusted for age (years), sex (female); spherical equivalent (dioptrre), mean arterial blood pressure (mmHg).

findings are in contrast to previous population-based studies in children and adults. Gopinath et al. (2010) observed in 1700 children with an age of 12-years that former low birthweight newborns had narrower retinal arterioles which is in accordance to other investigations in children (Mitchell et al. 2008). For adult individuals, an association between birthweight and retinal arteriolar calibre but not with retinal venular calibre was reported. The authors found an arteriolar calibre narrowing of 2.4 µm for each kg which was still significant after adjusting for multiple covariates including average arterial blood pressure measurement over 6 years (Liew et al., 2008). These results are in contrast to our data which may be caused by our younger cohort and potentially stricter blood pressure treatment regimes in the last years.

Our results are limited because 46% of all participants did not report their birthweight at study entry (Fieß et al. 2019). In addition, birthweight was self-reported and not validated by reviewing individual charts. Furthermore, missing data about gestational age and postnatal occurrence of retinopathy of prematurity may be confounders which have to be considered when interpreting our data.

In summary, this large population-based study shows no association between lower birthweight and central retinal venular equivalents, while the association for central retinal arterial equivalent was weakened by arterial blood pressure.

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Severe outcome of idiopathic inflammatory mass lesions primarily located in the posterior orbit and orbital apex

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Editor,

Idiopathic orbital inflammation (IOI) is a heterogeneous noninfectious inflammatory process that causes a mass or an enlargement of orbital