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Polymorphisms in thioredoxin genes are associated with prenatal thyroid hormone status in a cohort of high fish-eating pregnant women

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Iodine and selenium are required for synthesis of the thyroid hormones, thyroxine (T4) and triiodothyronine (T3), which are critical for optimal neurodevelopment[(1)]. Maternal T4 has previously been shown to positively correlate with child cognitive development in the Seychelles Child Development Study Nutrition Cohort 1 (SCDS NC1)[(2)]. The selenoproteins thioredoxin (*TXN*) and thioredoxin reductases (*TXNRD 1* and *2*) protect the thyroid from oxidative stress during hormone synthesis[(3)]. The aim of the present study was to investigate associations between single nucleotide polymorphisms (SNPs) in thioredoxin genes, *TXN* and *TXNRD*, with prenatal status of thyroid hormones in the SCDS NC1.

Blood was collected from pregnant women at enrolment and at 28 weeks gestation, from which serum concentrations of thyroid hormones were previously measured and genotyping performed for selected SNPs following leukocyte DNA extraction ($n = 170$). Univariate analysis of covariance (ANCOVA) was used to compare associations of each genotype with serum hormone concentrations, whilst adjusting for maternal age, BMI and smoking status. For *TXN*, homozygote minor and heterozygote alleles were combined.

		Thyroid hormones (pmol/L)							
		T4 enrolment		T4 28 wks		T3 enrolment		T3 28 wks	
Gene and Alleles	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE
***TXNRD1* (rs11111979)**									
Homozygous minor G/G	20	10·93	0·54	8·63	0·27	4·81	0·25	3·79	0·12
Heterozygous G/C	58	12·07*	0·32	9·04*	0·16	5·22	0·15	3·66	0·07
***TXNRD2* (rs5748469)**									
Homozygous minor A/A	19	11·31	0·59	9·19	0·29	4·93	0·27	3·93*	0·13
Heterozygous C/A	51	11·89	0·36	8·59	0·18	5·17	0·16	3·74	0·08
***TXN* (rs1049927)**									
Heterozygous G/A	12	13·24**	0·69	9·64*	0·35	6·07**	0·31	4·05*	0·14

Values are estimated means and their standard errors (SE). Significant differences in means between each allele compared to the reference genotypes for TXNRD1, 2 and TXN (CC, CC and AA respectively) are shown (*$P < 0·05$, **$P < 0·01$) from ANCOVA adjusting for maternal age, BMI and smoking.

Minor allele frequency of TXNRD1, TXNRD2 and TXN were calculated as 37%, 39% and 4% respectively. Variations of each genotype were significantly associated with greater concentrations of thyroid hormones. *TXNRD1* heterozygous was associated with T4 at both time-points, with *TXNRD2* homozygous being associated with T3 at 28 wks and *TXN* heterozygous with T4 and T3 at both time-points. Results indicate that genetic variation in *TXN* genes may influence prenatal thyroid hormone concentrations in this cohort of high-fish eating pregnant women. Further research should confirm these results in a larger cohort and investigate the influence of genetic variation in selenoproteins on neurodevelopment.

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