

Abstract title:

The impact of common *TMPRSS6* gene variants on iron status of pregnant women from rural Gambian

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Background

Anaemia is a global health problem that has a significant impact on women of reproductive age in low-and middle-income countries. Nutritional deficiencies, infection and genetic risk factors are the major drivers. However, the role of genetic factors particularly in settings where the prevalence of anaemia is high, has not been fully investigated. Genome-wide association studies have identified numerous single nucleotide polymorphisms in the *TMPRSS6* gene which are linked to impaired iron status in non-African populations. However, the impact of these SNPs on the risk of anaemia in West African populations have not been fully investigated.

Objectives

To investigate the effects of *TMPRSS6* rs2235321, rs4820268 and rs855791 on iron status biomarkers in pregnant Gambian women.

Methods

We analyse data from a cohort of pregnant (18 to 49 years, N=364), with genotype data on *TMPRSS6* rs2235321, rs855791 and rs4820268, and on iron biomarkers (serum iron, unsaturated iron binding capacity (UIBC), transferrin, ferritin soluble transferrin receptor (sTfR), transferrin saturation (TSAT) and total iron binding capacity (TIBC) and hepcidin) and hematology traits. We investigated the effects of genotype on these iron status indicators.

Results

The *TMPRSS6* rs223521 is associated significantly with reduced hepcidin levels (F ratio = 6.16, P=0.00235). The carriers of the minor allele (A) had decreased hepcidin concentration compared to GG carriers; AA vs GG = [mean (SE) 3.28 ng/mL (1.11) vs 5.44 ng/mL (0.62), P=0.0004]. Similarly, *TMPRSS6* rs4820268 significantly influenced serum iron levels (F = ratio = 3.58, P = 0.0289). Carriers of the rs4820268 minor alleles (GG) had decreased serum iron concentrations compared to AA

genotype carriers; GG vs AA = [mean (SE) 10.77 $\mu\text{mol/L}$ (1.40) vs 13.56 $\mu\text{mol/L}$ (3.13)]. No other iron phenotype was influenced by any of these two SNPs and no effect of rs855791 was observed on any phenotype.

Conclusion

TMPRSS6 rs2235321 may modulate hepcidin levels in pregnancy, whereas rs2235321 may predispose pregnant women to low iron status. Analysis of a larger dataset with more genetic markers associated with iron status may provide further insight into the functional effects of genetic variants within the iron regulatory genes on the risk of anaemia in African women of reproductive age. This may enable the development of genomic medicine approaches for the treatment and prevention of anaemia and iron related pathologies.

Keywords:

TMPRSS6 SNPs, Iron biomarkers, Pregnant women, Anemia