Obstetric and gynaecological features in females carrying variants in the skeletal muscle ryanodine receptor (RYR1) gene: a questionnaire study

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Abstract

Objective: To assess the impact of skeletal muscle ryanodine receptor (*RYR1*) variants, a common cause of neuromuscular disorders, on smooth muscle function, bleeding, obstetric, and gynaecological outcomes. **Design:** Questionnaire study. **Setting:** Online via the *RYR1*-Foundation patient support group covering countries across the world. **Population or Sample:** 154 women consisting of 66 *RYR1*-variant carrying participants and 88 controls. **Methods:** Online questionnaire designed to investigate symptoms of abnormal smooth muscle function, obstetric and gynaecological outcomes in women with *RYR1* variants. Questions were developed using a modified version of the MCMDM-1VWD questionnaire, and the NHS-heavy periods self-assessment tool. Obstetric and gynaecological symptoms explored include pregnancy-related complications, gestation length, parturition duration, post-partum haemorrhage and offspring birthweight. **Main Outcome Measures:** Bleeding scores were measured using a modified MCMDM-1VWD scale. Significance between groups were analysed using Fisher exact tests, Chi Square tests, and Welch's t-tests. **Results:** Women with *RYR1* variants exhibited a higher incidence of pathological bleeding scores ($p<0.0001$), severe menstrual bleeding, complications during pregnancy (preeclampsia and placenta praevia), post-partum haemorrhage, shorter pregnancies, frequent planned Caesarean sections, and offspring with lower birthweight, compared to controls. Gastrointestinal symptoms were also more common. **Conclusions:** *RYR1* mutated females exhibit a bleeding disorder and frequent gynaecological and obstetric complications. Considering their population frequency in otherwise pauci-symptomatic individuals, *RYR1* variants ought to be considered as a cause of otherwise unexplained menorrhagia and other gynaecological and obstetric manifestations. **Funding**: King's Health Partners Institute of Women and Children's Health **Keywords**: skeletal muscle ryanodine receptor *(RYR1)* gene; questionnaire; bleeding; menorrhagia; post-partum haemorrhage **Tweetable abstract**: RYR1 mutated females exhibit a bleeding disorder. RYR1 variants ought to be considered as a cause of otherwise unexplained menorrhagia, PPH and obstetric complications.

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