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Introduction: Differences of sex development (DSD) are congenital conditions characterized by atypical development of chromosomal, gonadal, and anatomical sex. Nuclear receptor subfamily 5 group A member 1 (*NR5A1*) plays a crucial role in transcriptional regulation of genes involved in steroidogenesis, adrenal and gonadal development. *NR5A1* emerged to be causative of 10 to 20% of 46, XY dysgenetic DSD.**Objective:** This study aimed to perform a systematic review evaluating the association between phenotype and genotype in patients with *NR5A1* defects and 46,XY DSD looking for outcomes of spontaneous puberty, gender change and social sex.**Method:** The systematic review was conducted in accordance with the Joanna Briggs Institute methodology for systematic reviews. We included studies with pathogenic, likely pathogenic and variants of uncertain significance (VUS) in the *NR5A1* gene in patients with 46,XY disorders of DSD. Embase, Medline and HGMD were our databases. Proportional meta-analyses were performed to calculate the overall frequencies.**Results:** Ninety-eight studies were included, encompassing 311 patients with 46,XY DSD due to *NR5A1* defects. Due to the imprecision of meta-analyses involving two or fewer patients, our primary analyses focused on those with three or more patients. The overall frequency of female sex-assignment was 54% (186 patients from 33 studies patients; 95% confidence interval (CI), 42-66%) and male was 46% (95% CI, 34-58%). The frequency of the missense variants was 54% (235 patients from 35 studies; 95% CI, 42-66%); for other variants such as nonsense, splicing, small indel and copy number variation, the frequency was 46% (95% CI, 34-58%). The frequency of the atypical genitalia was 85% (from 35 studies of 235 patients; 95% CI, 75-91%); and the female genitalia was 15% (95% CI, 09-25%); The frequency of spontaneous puberty was 74% (56 patients from 12 studies; 95% CI, 38-93%); and hypergonadotropic hypogonadism was 8% (95% CI, 03-17%); there were 10% of prepubertal gonadectomy (95% CI, 01-50%); The correlation between genotype/phenotype and phenotype/gender change was accessed using odds-ratios as a measure of effects, with no statistical difference (OR = 1.25; CI 95%, 0.56-2.77%) and (OR = 0.46; CI 95%, 0.08-2.73%), respectively. It's important to note that all gender changes were from female to male. The limited sample size, particularly in subgroup analyses, was a major limitation and may have impacted the statistical power of the findings.**Conclusion:** Patients with *NR5A1* variants exhibit significant phenotypic variability. The high frequency of spontaneous puberty highlights the need for caution in irreversible interventions during childhood, emphasizing individualized and multidisciplinary approaches to guide clinical management and gender assignment. Part of this study was support by FAPESP 2019/26780-9.

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Scenery and genotype-phenotype correlation of NR5A1 variants in 46, XY individuals with differences of sex development: a systematic review and meta-analysis