Background: Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders of adrenal steroidogenesis. CAH has 6 subgroups based on the affected enzyme. CAH due to 21-hydroxylase deficiency (21-OHD) accounts for 80-95% of the cases and is followed by 11β-hydroxylase deficiency (11-OHD) with a frequency between 0.2-8%. In the review, the frequency of classic 21-OHD in Turkish population is found out to be 1.7767 and the frequency of 11-OHD 1:38935.

Aim: The purpose of this study was to investigate genotype-phenotype correlation, clinical findings and long-term outcomes in patients with CAH due to 11-OHD and 21-OHD.

Subjects and Methods: The clinical records of 250 patients, followed in our clinic due to classic 21-OHD, non-classic 21-OHD and 11-OHD were analyzed retrospectively. 145 genetically proven 21-OHD and 11-OHD patients were included in this study. Endocrinological, clinical and molecular findings were recorded at presentation and follow-up. SPSS version 23 (Cicago, IL, USA) was used for statistical analyses.

Results: Some clinical findings of the patients are summarized in Table 1. Out of 145 patients diagnosed with CAH, 122 had (83.6%) 21OHD, 66 salt wasting (SW), 40 simple virilizing (SV), 16 non-classic (NC); 23 (16.4 %) had 11-OHD. SW 21-OHD was the most common and the earliest diagnosed CAH type. Consanguinity rate was high in all groups(47%, 45% and 69.6%, respectively). Due to severe virilization and late diagnosis, some of the XX patients were raised as male.3 (7%) in SW, 6 (21.4%) in SV, and 3 (25%) in 11-OHD. Frequency of SGA was higher in SV and NC 21-OHD (p<0.048). While 29 different mutations were detected in 21 OHD, there were 12 different mutations in 11-OHD. The most common mutation was IVS2-2 T>T in only the all patients with 21-OHD, but also in the SW (34.7%) and SV (34.4%). Furthermore, the most common mutation in 21-OHD was p.V37G (34.4%) and p.Leu299Pro (25%) in 11-OHD (Figure 1). Positive predictive value (PPV) for all 21-OHD patients was 78.4%, PPV in subgroups according to enzymatic activity was 80.8% in group (Null +Enzyme activity 0%), 100% in group (1), 62.5% in group B (1%), and 65.2% in group C (20.5%). There was no genotype-phenotype correlation in patients with 11-OHD. 53.3% of patients in 21-OHD and 69.6% in 11-OHD had reached the adult height. Mean value of the difference between the adult height and the target height for those, who have reached adult height was 0.42±0.17 in SW, -0.91±1.35 in SV, -0.140±0.94 in NC, and -0.71±0.14 in 11-OHD. The pubertal spurt was not sufficient in classic 21-OHD (Figure 3.3.4). In logistic regression, the most important factor on short stature was height at onset of puberty (p=0.018, B=3.058). The early rate of puberty was 24.2 % in SW, 40% in SV, 18.8% in NC 21-OHD and 56.5% in 11-OHDPc0.003 in all groups). Frequency of testicular adrenal rest tumour (TART) was 29.4% for SV, 33.3% for SW and 40% for 11-OHD (Figure 5). While the puberty rate in all subgroups in 21-OHD(32.8% in SW, 33.3% in SV, 31.2% in NC) was significantly high, it was low in the 11-OHD (5%) (p<0.01).

Conclusion

In Turkey, where there is a high rate of consanguinity, the frequency of 11-OHD is also high.

The rate of mutation diversity for both 21-OHD and 11-OHD was very high. The positive predictive value of genotype-phenotype correlation in 21-OHD was good.

The pubertal spurt was not sufficient in classical 21-OHD.

While the rate of obesity development was high in 21-OHD, the prevalence of TART and early puberty were higher in 11-OHD.

Detection of the frequency of mutations may be important for early diagnosis, prenatal diagnosis and treatment, and establishing a screening strategy.

References