THE SPECTRUM OF CLINICAL AND MOLECULAR FINDINGS IN 212 SAUDI PATIENTS WITH 21-HYDROXYLASE DEFICIENCY

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BACKGROUND

21-hydroxylase deficiency is an autosomal recessive inherited disorder that affects the adrenal glands. The adrenal glands are located on top of the kidneys and produce a variety of hormones that regulate many essential functions in the body. In people with 21-hydroxylase deficiency, the adrenal glands produce excess androgens, which are male sex hormones. 21-α hydroxylase deficiency (21OHD) accounts for over 90% cases of CAH. This enzyme is encoded by CYP21A2 gene, on chromosome 6p21.3. 21OHD results in aldosterone and cortisol deficiency. There is excessive accumulation of 17-hydroxyprogesterone (17OHP) and other steroid precursors which are shunted into androgen synthesis pathways. There is a wide variation in the phenotype depending on the type of mutation in CYP21A2 gene. Large deletion, nonsense or frameshift mutations that result in complete absence of 21- hydroxylase activity produce salt wasting forms of CAH while mutations resulting in even 1-2% enzyme activity, allow sufficient aldosterone formation and lead to only virializing form of CAH. In this study, we report our findings of the clinical features and molecular genetics of a series of Saudi patients with CYP21A2 deficiencies.

OBJECTIVES

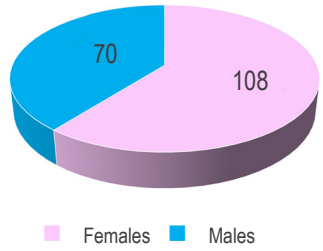
1 - To review the clinical presentation of the disease in the 212 saudi patients diagnosed with 21-hydroxylase deficiency.
2 - To review molecular findings of the 212 Saudi patients to find out the most common mutations within this group.
3 - To find out what the families of the affected children and the adults patients have preferred as preventetive options after receving genetic counseling.

METHODS

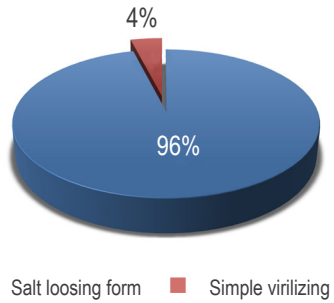
This study is a Quantitative study. It was conducted at King Faisal Specialist Hospital& Research Center. It included a total of 212 Saudi patients diagnosed with 21-hydroxylase deficiency. All Saudi patients between the age of 0–45 years who tested positive for mutations causing the disease. All the data was collected between June 2015 – June 2021.

RESULTS

TOTAL 178

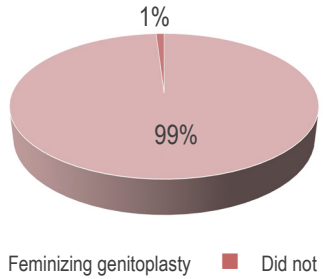


The most common type of 21-hydroxylase deficiency

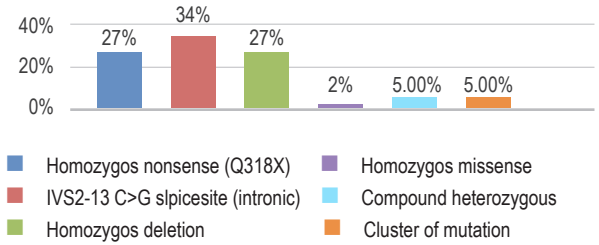


- ☐ 97.3% were consanguineous.
- ☐ In our study, most of our female participants with the salt wasting form presented very early in her neonatal period with ambiguous genitalia and salt wasting.
- ☐ Most of our male patients with the salt wasting manifested the disease since birth or within few months.
- ☐ They presented with vomiting and lethargy.
- ☐ The hormonal profile was consistent with the diagnosis of CYP21A2 deficiency with high 17-hydroxyprogesterone and elevated serum ACT, flagged to have hyponatremia, hyperkalemia and elevated17-hydroxyprogesterone.

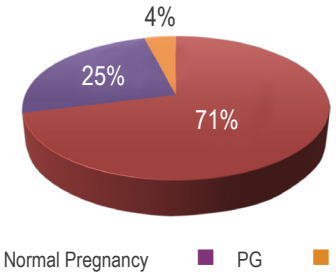
The percentage of females who went through the feminizing genitoplasty



The most common mutation



The most preferred preventative option



DISCUSSION

Our findings demonstrate 34% of our patients had the IVS2-13 C>G splice site (intronic) mutation.

- ☐ 27% of our patients had the homozygous nonsense mutation.
- ☐ 27% of our patients had the homozygous deletions.
- ☐ In a study done on 2021 in Cuba ,Point mutations were identified in 56% patients.
- ☐ Also, a high correlation was observed between the Q318X mutations with the classic forms.
- ☐ The majority of the patients presented with the classical salt loosing form.
- ☐ Simple virilizing form was present only with missense mutations in our study.
- ☐ In the study in Cuba the great majority of patients who presented combinations of two serious mutations, the SW form was established.
- ☐ Also the majority of patients with two mild mutations demonstrated the NC form of the disease.

CONCLUSION

- ☐ Our data implies that most of our patients had the classical Salt-wasting type of the disease.
- ☐ Most of our patients were from consanguineous families.
- ☐ Some of the families had more than one A.R genetic condition in the family.

Most of the families preferred not to go for preventative options because of no clear Fatwa of terminating affected children with this condition and not all the families are eligible for PGD.