Sibs Of Iraqi Families Affected by Congenital Adrenal Hyperplasia

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Summary:

Background: *Congenital adrenal hyperplasia (CAH) is inherited disorders in which defects occur in one or more of the enzymatic system involved in cortisol biosynthesis.*
Patients and Methods: *Sixteen families which had sibs with Congenital Adrenal Hyperplasia were included in the study. The patients have been divided into three groups based on the type of enzyme defect:*
group I: (4 males and 3 females) were newborn babies, suffering from a complete defect in the enzyme 21- hydroxylase, the clinical syndromes of them were presented with ambiguous genitalia, salt-loosing, vomiting, dehydration and failure to survive.
Group II: (17 females and 2 males) ranging in age from 7 - 30 years.This group of patients were suffering from a partial defect in the enzyme 21-hydroxylase. The clinical syndromes of affected females were hirsutism, deeping of the voice, primary amenorrhea and primary infertility, while male patients represented with precocious puberty.
Group III: (4 patients, 3 sons of the same family and one from other family). They are all males ranging in age from 2 - 8 years. They were suffering from a partial defect in the enzyme 11β-hydroxylase.
Results: *The 16 families studied had thirty sibs (sisters and brothers) affected with congenital adrenal hyperplasia (CAH), some of these families had two affected sibs, others had three. Some sibs had a defect in the enzyme 21-hydroxylase (the classical form), other had a defect in the enzyme 11β-hydroxylase while the third type of sibs had a defect in both enzymes. The clinical symptoms were a moderate increase in blood pressure and precocious puberty.*
All patients had low cortisol levels together with elevated urinary 17-ketosteroid levels. The final diagnosis of all groups was based on the elevated levels of pregnanetriol and 11-oxygenation Index, the latter was found highly elevated especially in Group III patients.
Conclusion: *Sibs from the same family are affected with the enzymes (21-OH), (1-13, 15 & 23), while other sibs had a defect in the enzyme (11β-OH).*
This abstract is not structured. I have structured it, but it still needs an objective.
Keywords: *congenital adrenal hyperplasia (CAH), sibs, 21-hydroxylase, 11β-hydroxylase.*

Introduction:

Congenital adrenal hyperplasia (CAH) is inherited disorders in which defects occur in one or more of the enzymatic system involved in cortisol biosynthesis.
The enzyme deficiency leads to a reduction in cortisol secretion and hypertrophy of the adrenal cortex. In these cases the adrenal cortex is over activated because of the negative feed-back mechanism ,which results in a compensatory rise in corticotrophin secretion and accumulation of cortisol precursors, particularly 17α-hydroxyprogesterone (17α–OHP), and excessive production of androgens which give rise to various degrees of virilization (1, 2, 3 & 4).

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There are four recognized clinical forms of (CAH): salt-loosing or wasting (SW) which is a complete defect in the enzyme 21-hydroxyls (5, 6, & 7). The second group is the simple degree of virilisim (SV) (1, 4, & 8). The third group is the non-classical form (NC) or the late-onset (attenuated and acquired) defect appears later on after puberty (9, 10, 11, 12, & 13).

While the fourth group is the defect in the enzyme 11β-hydroxylase, the clinical syndromes usually a moderate increase in blood pressure and simple virilisim (14, 15, & 16).
The majority of cases (90% of the reported cases) were associated with 21-hydroxylase deficiency and to a lesser extent the defect (10% of the cases) in the enzyme 11β- hydroxylase (1, 3, 5, 17 & 18).
The defect in 21-hydroxylase (21-OH) is correlated with extent of defect in the cortisol pathway, hence 17α-hydroxyprogesterone is not converted to 11β-hydroxy cortisol which is a good precursor for androgen (1, & 4). An accumulation of its precursor 11-deoxycortisol metabolite may be found in urine together with a large amount of 11-nonoxygenated

17-oxosteroids. Pregnanetriol may be moderately increased in urine (17, 18, 19 & 20). The over production of these precursor metabolites are excreted in large amounts in urine. The study of these metabolites gives a good indication of the nature of the affected enzymes (16 & 20).

Materials and Methods:

Patients: Sibs of 16 families (30 brothers and sisters, 10 males and 20 females), ranging in age from newborn babies up to 30 years. They are represented with precocious puberty for males and virilization for females and with salt losing, vomiting, and failure to survive for the newborn babies.

Methods: Twenty four hour urine samples were collected from each patient, and were preserved with chloroform, stored at –15°C until the time of analysis. Urinary 17-oxosteroids were determined by the method recommended by the Medical Research Council (1963), and pregnanetriol (P-triol) by the method of Brooks and Prunty (1960). The 11- oxygenation index (11-OI) was determined by the method used by Edward et.al (1964) (20, 21 & 22).

Results:

The statistical summary of the urinary steroids (17-OS), (P-Triol) and (11-OI) are shown in Tables (1-3).

Group I: All newborn babies affected with complete defect in the enzyme 21-hydroxylase, they were excreting a moderate amount of (17-OS), (P-Triol) and (11-OI) as are shown in Tables (1-3) $p<0.01$.

Group II: Patients suffering from a partial defect in the enzyme 21-hydroxylase. They were excreting large amounts of urinary steroids, especially for (17-OS) and (P-Triol), while a moderate increase in (11-OI) as indicated in tables (1-3), $p<0.01$.

Group III: Patients suffering from partial defect in the enzyme (11β-OH). They were excreting a moderately high (11-OI) as shown in Table (3), $p<0.01$.

Tables (1 – 3) show a summary of the statistical analysis of (17-OS), (P-Triol) and (11–OI), with patient groups mean values and percent points of variance-ratio (F) distribution.

Table (1): Statistical summary analysis of the data of urinary 17-OS of the groups of patients

Groups	mean in mg/TV	LSD0.05	P
Group I	1.6	Gr.I vs.Gr.II = 0.92	< 0.01
Group II	12.74	Gr.I vs.Gr.III = 1.33	< 0.01
Group III	5.91	Gr.II vs.Gr.III = 1.19	< 0.01

TV = total volume of urine sample (24 hours)

Table (2): Statistical summary analysis of the data of urinary P-Triol of the groups of patients

Groups	mean in mg/TV	LSD 0.05	P
Group I	1.06	Gr.I vs.Gr.II = 4.11	< 0.01
Group II	3.75	Gr.I vs. Gr.III = 4.65	< 0.01
Group III	0.29	Gr.II vs.Gr.III = 5.68	< 0.01

Table (3): Statistical summary analysis of the data for urinary 11-OI of the group of patients

Groups	mean Ratio	LSD 0.05	P
Group I	1.59	Gr.I vs. Gr.II = 0.92	< 0.01
Group II	1.2	Gr.I vs. Gr.III = 1.33	< 0.01
Group III	7.45	Gr.II vs.Gr.III = 1.19	< 0.01

Discussion:

CAH is a rare defect over all the population, its diagnosis is based upon the clinical features of the patients and on the abnormal excretion patterns of the urinary steroid metabolites. The clinical syndromes of patients with CAH are including: virilization of girls with precocious puberty of boys, together with salt –losing or dehydration for the newborn babies (1, 3, & 4). Thus, the values of (11-OI) of the three groups as is indicated in table (3), differ from each other depending on the defect in the type of the enzyme (4, 5, & 15). The results presented seem that they were highly significant between groups of patients ($p<0.01$), as shown in table (3). This result is in agreement with those reported by other workers (16 & 20). Whereas, values obtained for both (17-OS) and (P-Triol) were highly significant among the groups of patients ($p<0.01$), as indicated in tables (1 & 2). These results were in agreement with previous works reported by (1, 4, 11, 12 & 15).

In conclusion, this study revealed that sibs from the same family are affected with the enzymes (21-OH), (1-13, 15 & 23), while other sibs had a defect in the enzyme (11β-OH), (14, 15 & 16).

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