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Original Research Paper

Endocrinology

CLASSICAL CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY IN TERTIARY CARE CENTRE IN KASHMIR VALLEY BETWEEN 1997 AND 2017

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ABSTRACT

Aims: To evaluate the incidence, gender, symptoms and age at diagnosis among patients with congenital adrenal hyperplasia (CAH) presenting to a tertiary care hospital.

Methods: Data were collected retrospectively for all CAH diagnosed patients between 31.07.1997 and 31.06.2017 and were compared with the data of the previously conducted studies evaluating CAH patients discovered between 1964 and 1984.

Results: During 20-year period, 30 classical CAH patients presented. There were 13 salt-wasting (SW) (8 females/ 5 males) and 17 simple virilizing (SV) patients (16 females/ 1 male). The lower incidence of SW boys compared to SW girls (8: 5) indicate that substantial proportion of SW boys die unrecognized. health care, diagnosis was established significantly earlier in SW and SV girls. During 1995–2006, none of the patients died following the diagnosis of CAH, and there was no erroneous sex assignment.

Conclusion: Despite of improvement in health care, diagnosis of CAH in developing world is still delayed and some of the patients go unrecognized or die. Therefore, we think that the results of our study support the need for the introduction of newborn screening.

KEYWORDS :

INTRODUCTION:

Congenital adrenal hyperplasia (CAH) is an autosomal recessive inherited disorder resulting in the loss of activity in one of the enzymes necessary for adrenal steroidogenesis. Deficiency of 21-hydroxylase (21-OHD) is the most common cause of CAH. Depending on the degree of the 21-OH impairment, the disease is characterized by decreased cortisol and aldosterone production and excessive androgen production. Complete 21-OHD or the salt-wasting (SW) form causes a life-threatening metabolic crisis during the first weeks of life. The simple virilizing (SV) form presents with precocious pseudopuberty in both sexes. Both classical forms of CAH (SW and SV) lead to prenatal virilization of female fetuses. Mild 21-OHD results in the nonclassical (NC) form, characterized by hyperandrogenism presenting later in childhood or in early adulthood. Early recognition of CAH might prevent life-threatening adrenal crisis, enable correct gender assignment at birth and prevent postnatal virilization, growth acceleration and premature pubarche [1]. A large proportion of patients with the classical form of CAH are clinically recognized soon after birth, but in certain number of patients, especially male, diagnosis is missed. Therefore, many countries have included CAH in their neonatal screening programs based on measurement of 17-hydroxyprogesterone (17-OHP) in dried blood spots. We conducted a retrospective study of all classical CAH patients who attended hospital from 1997 to 2017. The results of our study were compared with the data of the previously conducted study evaluating all CAH patients discovered and treated between 1964 and 1984 in one referral center, in which over 85% of all CAH patients in Croatia were diagnosed and treated [4] . Finally, we reevaluated the current bases and the need for the introduction of neonatal screening for CAH in developing countries.

MATERIAL AND METHODS:

Data on all CAH patients who presented between 31-07-1997 to 31-06-2017 were collected. Endocrinologists who provided care for patients with CAH completed a questionnaire evaluating clinical and laboratory data at diagnosis, family history and data on prenatal diagnosis. The diagnosis of CAH was based on typical clinical symptoms and laboratory findings (sodium, potassium, 17-OHP, androstenedione, testosterone, plasma renin activity) and was confirmed by analysis of the CYP21 gene.

Statistical analysis of collected data was performed using the $\chi 2$ median test. $p < 0.003$ was considered statistically significant.

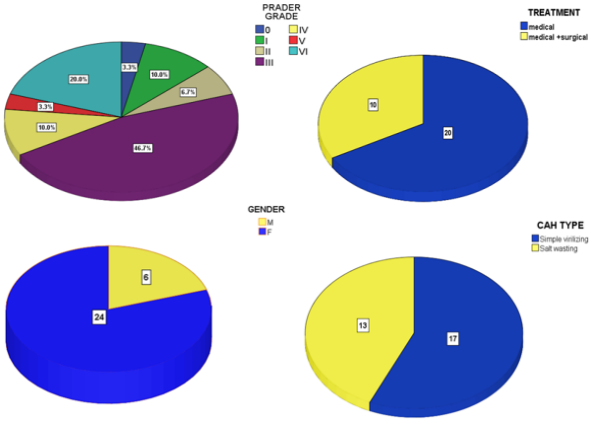
RESULTS:

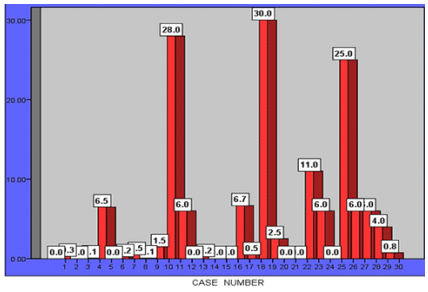
During the 12-year period, 30 patients with classical CAH due to 21-OHD were diagnosed at the hospital. There were 13 SW (8 females and 5 males) and 17 SV patients (1 male and 16 females).

With 30 cases registered and all having average of more than 13 years follow, we had 24 females and 6 males.Out of 30 cases we had 17 simple virilising and 13 were salt wasting.The average age of presentation in salt wasting boys was 4 weeks and in salt wasting girls 8 weeks. Presentation age in simple virilising boy was 6.5 years and in simple virilising girls as 6.4 years. The mean level of 17OH progesterone was 58.3 ng/ml and minimal level of testosterone was10 ng/ml and maximum level was 435 ng/dl (figure 1). There was positive family history in only 10 cases. Prader staging , mode of treatment and other parameters are depicted in figure 2 and 3.

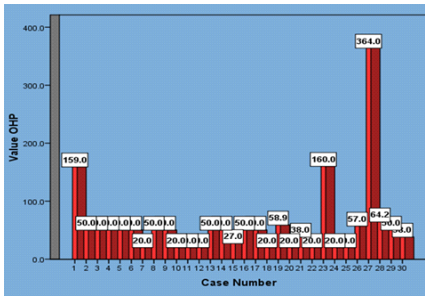
CLASSIC CAH 1995-2006 *Katja dumic et al Horm Res 2009;72:310-314*		SKIMS	
NO OF CASES	34	30	
DURATION OF FOLLOW UP	12 YEARS	MEAN 3.97 YEARS (RANGE 0.5 -13 YEARS)	
GENDER	BOYS 15 GIRLS 19	BOYS 6	GIRLS 24
SALT WASTING BOYS	8	5	
SALT WASTING GIRLS	12	8	
SIMPLE VIRILIZING BOYS	7	1	
SIMPLE VIRILIZING GIRLS	7	16	
Mean age of diagnosis	**mean range**	**MEAN**	**RANGE**
SALT WASTING BOYS	3.8 WEEKS (1-8WEEK)	4 WEEKS	(4-12)
SALT WASTING GIRLS	3 WEEKS (3-21 D)	8 WEEKS	(0 – 15 WEEKS)
SIMPLE VIRILIZING BOYS	4.8 YEARS (3.1-9.2 Y)	6.5 YEARS	--
SIMPLE VIRILIZING GIRLS	7.2 MONTHS (1-16 M)	6.4 YEARS	(0 - 30 YRS)

Figure 1.





Age at presentation



Level of 17OHP in CAH patients (Figure 2 and 3)

DISCUSSION:

We conducted a study in order to evaluate gender distribution and clinical characteristics of patients and to estimate the validity of the existing health care system in early identification of patients with CAH [6, 8]. We also found that the diagnosis was established significantly later among SV boys (average age of 6.5 years) with advanced growth and pubertal development. The lower number of SW boys compared to SW girls (5,8) and almost equal number of SW and SV boys (5,1) supports the well-known finding that a substantial proportion of SW boys die unrecognized during an adrenal crisis [8–13]. Among SV patients, it has been observed that the diagnosis is missed more often in boys; therefore, there are more female than male SV patients (16, 1) [6,10].

Besides a more accurate prediction of incidence of disease, the introduction of neonatal screening for CAH brings many other advantages: detection of patients that would otherwise be missed, earlier diagnosis, reduction of the number of adrenal crises and incorrect sex assignments, decrease in number of cases with postnatal virilization, precocious puberty and growth acceleration, and improvement of clinical symptoms.

The method of 17-OHP measurement in dried bloodspot was introduced in multiple countries and has been used for rapid 17-OHP measurement in patients suspected to have CAH based on their clinical symptoms. The screening infrastructure already exists in many countries as newborn screening is performed for phenylketonuria and congenital hypothyroidism with sample collection on the 3rd day of life. Therefore, screening for CAH could be added to the existing screening programs, which would reduce the costs of collection and delivery of the samples.