P3-P005

Age at Diagnosis and Outcome in Maghreb patients with 21-hydroxylase Deficient Congenital Adrenal Hyperplasia; Urgent need for Newborn Screening

Asmahane Ladjouze[a] , Imane Yala[a] , Manel Yahiaoui[a], Dounia Zerguini[a] , Veronique Tardy[b] , Kahina Mohammedi[a] , Ourida N Taleb[a] , Soraya Kerkouche[a] , Karima Berkouk[a] , Manoubia Bensmina[a] , Abdeljlil Maoudj[a] , Rawda Aboura[a] , Tahar Anane[a] , Yves Morel[b] & Zahir Bouzerar[a]

[a]Department of Paediatrics, Bab El Oued Teaching hospital, Algiers, Algeria; [b]Service d'endocrinologie Moleculaire, Hospices civils de Lyon, Lyon, France

Background

Congenital adrenal hyperplasia (CAH) owing to 21-hydroxylase deficiency (21OHD) is an autosomal disorder of impaired adrenal cortisol biosynthesis with associated androgen excess. This disease that can lead to severe salt wasting during the neonatal period is now included in most developed countries new-born screening programs.

In the absence of such newborn screening, the clinical diagnosis alone of classic CAH might be delayed or misinterpreted and salt-wasting crises could cause neonatal deaths. Moreover, when the diagnosis is delayed, there is an increased risk of psychomotor delayed as a consequence of severe hypoglycaemia and hyponatremia.

AIM

To examine age at presentation and outcome in children diagnosed with 21-hydroxylase deficient congenital adrenal Hyperplasia (21-OHD CAH) in Algeria in the absence of a national neonatal screening program.

DESIGN

This was a retrospective analysis of patients followed in a single centre from 2007 to 2017. The diagnosis of CAH was established on clinical and biochemical grounds ± genetic analysis. Statistical analysis was done with Epi-info 7 (CDC) software

RESULTS

Prevalence Of 21-OH CAH: In our cohort of CAH (186 patients from 165 families) 21-OHD CAH was diagnosed and confirmed by clinical and biological grounds in 168 patients from 145 families, rendering it the most common of CAH before 3 beta-hydroxysteroid-dehydrogenase deficiency (12 patients from 8 families) and 11-hydroxylase deficiency (6 families, 8 patients).

Of 168 patients, 114 were Females (F) and only 54 were males (M), Sex Ratio **was** 1M/2F. Consanguinity was found in 61% of the cases.
The classical salt-wasting form (SW) of 21-OHD CAH was most common (80%) comprising 135 (66%F) patients, while 31 patients (77%F) had simple virilising (SV-21OHD CAH) and 2 Females had non-classical (NC-21OHD) CAH (cf Fig.1 and 2).

Initial referral (cf Fig.3) was with disorder of sex development (DSD) in 27% (all Females), dehydration in 28% (6% males); the association of DSD and Dehydration in 35% (100% Females); sexual precocity (7%) and family history of CAH. At presentation, DSD was found in all but 4 46,XX patients (2 NC-21OHD and 2 treated prenatally). Severe hyponatremia and dehydration occurred in 86 (51.5%) neonates both in males and females (61 vs 45%, p=0,06).

Ages at presentation and at the initiation of hydrocortisone (Table.1) were significantly later in males than females (191± 524 vs 83±333 days and 268±639 vs 153±512 days, p<0.001), attributable to DSD being the presenting feature in the latter. Mean age at diagnosis was significantly earlier in the SW (51±136 days) than in the SV 21-OHD (617.9±937 days). Fludrocortisone (being unavailable in Algeria) was started in 148 patients at 140±308 days (vs 118±406 days for hydrocortisone in all patients.

Mean plasma Sodium at diagnosis (Table 2) was lower in males than females (118±11 vs 123±10 meq/l, p<0.03) and between the SW and the SV 21-OHD (120±10 vs 130±3 meq/l, p<0.01)

Hormonal data (Table 2): 17OH-Progesterone (17OHP) was elevated in all patients (1672±3048 nmol/l), there was no significant difference between both sexes and between the 2 classical forms. Renin was significantly higher in the SW 21-OHD (2817±6483 vs 153.2±165 pg/ml).

Sex assignment: 62 of 114 (54,4%) 4,XX patients were initially assigned as males, mean±SD (range) at reassignment was 3.8± 8 -0-36) months in 58 patients with 4 46,XX patients raised as males according to parental wishes.

Treatment: All patients were treated with hydrocortisone, 148 (88%) were initially treated with Fludrocortisone. Only 30,8% of the females had undergone surgery at a mean± SD (range) age of 3,6±4,5 (0,5-10) years

Clinical outcome (Table 3): Since diagnosis, 8 (4,7%) patients have died in adrenal crisis. Mean age at last visit was 5.3±4 years. More than one third (37.5%) of the Patients have presented at least one episode of dehydration since diagnosis, 24% have advanced bone age, 14% have been treated with LHRH agonists and 13% with growth hormone, 8 males have testicular calcifications and 3 patients have adrenal calcifications. Finally, of 89 patients aged >4 years, 18 (20%) have moderate to severe mental delay

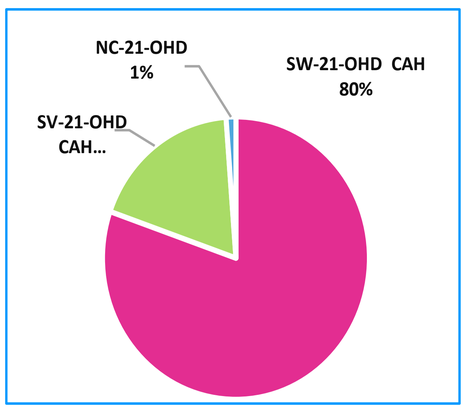

Fig 1. Frequency of each form of 21-OH CAH

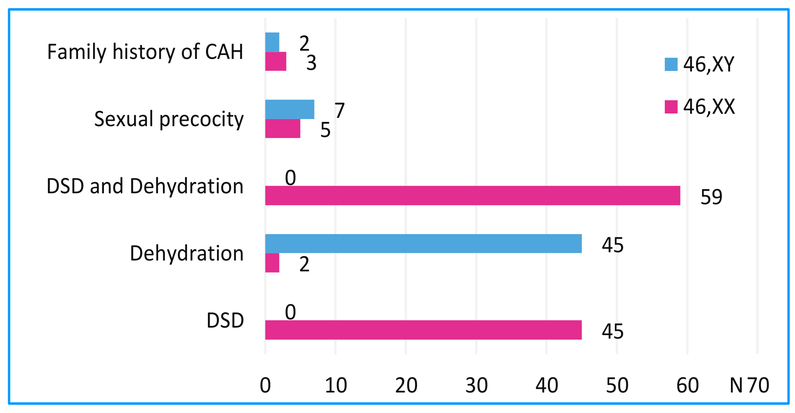

Fig 3. Cause of initial referral according to karyotype

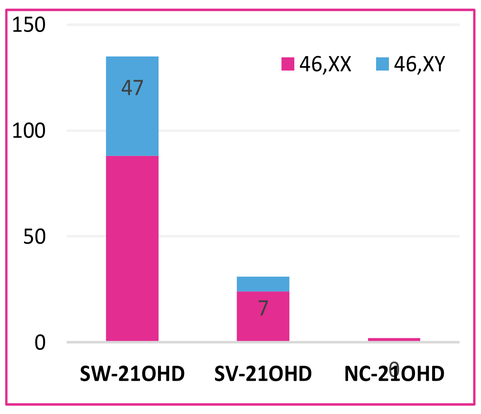

Fig 2. Frequency each form of CAH according to karyotype

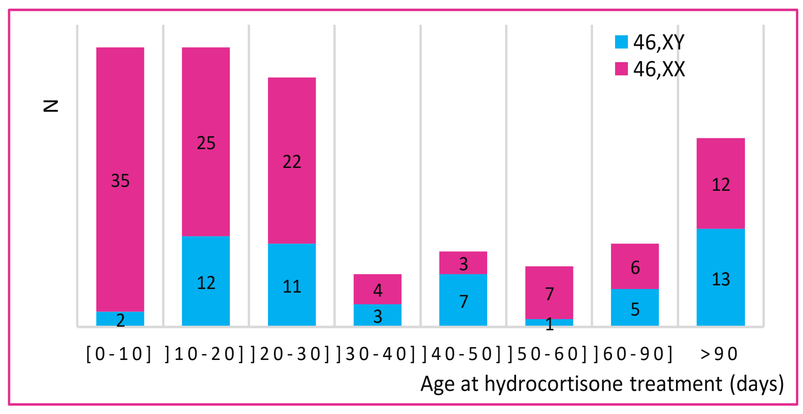

Fig 4. Age (days) at the initiation of hydrocortisone treatment

Table 1. Age (days) at presentation and initiation of hydrocortisone treatment according to sex and form

	Age at presentation				Age at the initiation of treatment (days)		
	N	Mean±SD	Median (Min-Max)	p	Mean±SD	Median (Min-Max)	p
46,XX	114	82.5±333	4.5(0-2485)	P<0,001	152.6±512	20 (0-3150)	P<0,001
46,XY	54	191.5±524	28.5(5-2920)		267.9±639	36(8-3540)	
SW-21OHD	135	25.2±45	15(0-390)		51.4±136	23(0-1460)	P<0,001
SV-21OHD	31	444.5±756	7(0-2920)	P<0,001	617.9±937	30(0-3540)	
SV-21OHD	2	1273.5±1713	1273.5-62-2485)		2882.5±378	2882.5(2615-3150)	
All patients	168	117.5±406	15 (0-2920)		189.7±557	23.5 (0-3540)	

Table 2. Biological and hormonal data

Biological and Hormonal data	N	Mean± SD	Median	Range	Reference range (neonates)
Na at diagnosis (meq/l)	132	120.9±10,3	122	93-142	135-145
Max 17OHP(nmol/l)	136	1672.7±3048,6	684	100-200509	1,5-40
Delta4A (ng/ml)	142	10.3±22	2,9	0.05-210	0.21-3.08
Testosterone (nmol/l)	154	10.3±26,3	1,7	0.006-223	
ACTH (pg/ml)	51	248.2±341	119	5-1557	29-38
Renin (pg/ml)	124	2323±5939	320	1.13-35500	6-61

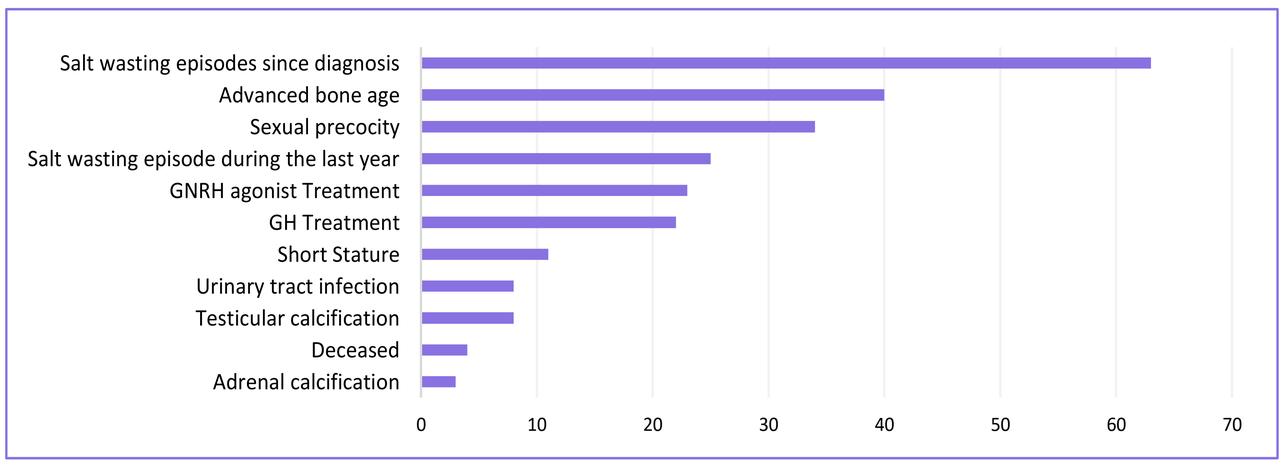

Fig 5. Clinical Outcome

CONCLUSIONS

Currently, males with 21-OHD are diagnosed half often as females, reflecting death from SW during the first few weeks. Delay age at diagnosis causes severe hyponatremia in SW patients which increasing the risk of mortality and developmental delay. National screening for CAH in Algeria and all Maghreb countries where consanguinity rate and hence CAH prevalence high is urgently required

Nothing to disclose concerning this presentation