A New International Registry Highlights The Differences In Practice For Reaching A Diagnosis Of CAH

[1]Mariam Kourime, [2]Jillian Bryce, [2]Jipu Jiang, [3]Nayananjani Karunasena, [4]Birgit Koehler, [5]Tulay Guran, [6]Sabine Elisabeth Hannema, [7]Martine Cools, [8]Hedi L. Claahsen Van Der Grinten, [9]Carlo Acerini, [10]Berenice B Mendonca, [11]Nils Krone, [12]Feyza Darendeliler, [13]Mona Ellaithi, [14]Silvano Bertelloni, [15]Antonio Balsamo,[16]Lidka Lisa, [17]Walter Bonfig, [18]Anna Nordenstrom,[19]Heba Elsedfy, [20]Olaf Hiort, [21]Lallemand Dagmar, [22]Otilia Marginean, [3]Richard Ross, [2]Syed Faisal Ahmed.

[1]Abderrahim Harouchi Children's University Hospital, Casablanca, Morocco, [2]University of Glasgow, Glasgow, UK, [3]University of Sheffield, Sheffield, UK, [4]Charite Paediatric Endocrinology, Berlin, Germany, [5]Marmara University, Istanbul, Turkey, [6]Leiden University, Leiden, The Netherlands, [7] Ghent University, Ghent, Belgium, [8]Radboud University Medical Centre, Nijmegen, The Netherlands, [9]University of Cambridge, Cambridge, UK, [10]University of São Paulo, São Paulo, Brazil, [11]University of Birmingham, Birmingham, UK, [12]Istanbul University, Istanbul, Turkey, [13]University of Khartoum, Khartoum, Sudan, [14]University Hospital Pisa, Pisa, Italy, [15]University of Bologna, Bologna, Italy, [16] Institute of Endocrinology, Prague, Czech Republic, [17]Munich Technical University, Munich, Germany, [18]Karolinska University Hospital, Stockholm, Sweden, [19]Ain Shams University, Cairo, Egypt, [20]University of Lübeck, Lübeck, Germany, [21]Childrens Hospital of Eastern Switzerland, St Gallen, Switzerland, [22]University of Medicine and Pharmacy "Victor Babes" Timisoara, Timisoara, Romania.

Introduction:

Following the 2010 CAH consensus, the need for genetic confirmation of diagnosis remains uncertain and variation in practice is unclear.

Objective: To assess the variation in practice for reaching a diagnosis of CAH using I-CAH Registry

Methods:

- This variation was assessed by using the International CAH(I-CAH) Registry which was developed using the same platform as the I-DSD Registry.
- The cases in whom the diagnosis was based on genetic confirmation were compared to those who had solely biochemical confirmation considering different variables: median year of birth, age at first presentation, date of addition in the I-DSD/I-CAH Registry, and the centres adding these cases

Results and Conclusions:

- After the development of the I-CAH Registry in October 2014:
  - The number of centres adding CAH cases has doubled (Figure1)
  - The rate of addition of CAH cases increased by10 fold from 2/month to 21/month.
  - The number of cases added per year and shared internationally has increased by 6 fold (Figure2&3) .
- By May 2016, of 2095 cases, there were 604 CAH cases (28%).
- The median year of birth of CAH cases was 2003 (1937,2016) and 231(38%) were over 16yrs old.
- The median age at first presentation was 1month(1 m,48yrs) and the aetiology of CAH was 21-hydroxylase deficiency in 556(92%).
- Of the 604 cases, 376(62%) were 46,XX and 9(2.5%) of these cases were raised as boys. The median age at presentation of these 9 cases was 9months(1m,18yrs).
- Of the 604 cases in the I-CAH Registry, 447(74%) cases were displayed in our consent level and information concerning the basis of diagnosis were available in 215 (50%)cases. The majority of these cases were confirmed genetically 109(65%) and only half of this number was confirmed solely by biochemistry.(Figure5).
- The cases confirmed genetically were younger than those with biochemical confirmation (Table).
- The majority of cases confirmed genetically were added by European centres whereas the non-European centres added mainly cases confirmed by biochemistry alone (Table).
- The temporal shift in practice toward molecular confirmation was also demonstrated by the earlier upload date of cases without genetic confirmation compared to those with genetic confirmation in whom the annual rate of addition has significantly increased recently.
- This study shows that the creation of the I-CAH Registry has increased the number of CAH cases shared internationally and strengthen the potential of international research.
- The I-CAH Registry has also improved the quality of data in CAH patients with availability of more cases confirmed genetically who are eligible for studies assessing the outcome in relation to phenotype.

References:

Phyllis W. Speiser, Ricardo Azziz, Laurence S. Baskin, Lucia Ghizzoni,Terry W. Hensle, Deborah P. Merke, Heino F. L. Meyer-Bahlburg et al.

A Summary of the Endocrine Society Clinical Practice Guidelines on Congenital Adrenal Hyperplasia due to Steroid 21-Hydroxylase Deficiency. Int J Pediatr Endocrinol2010; 2010: 494173.

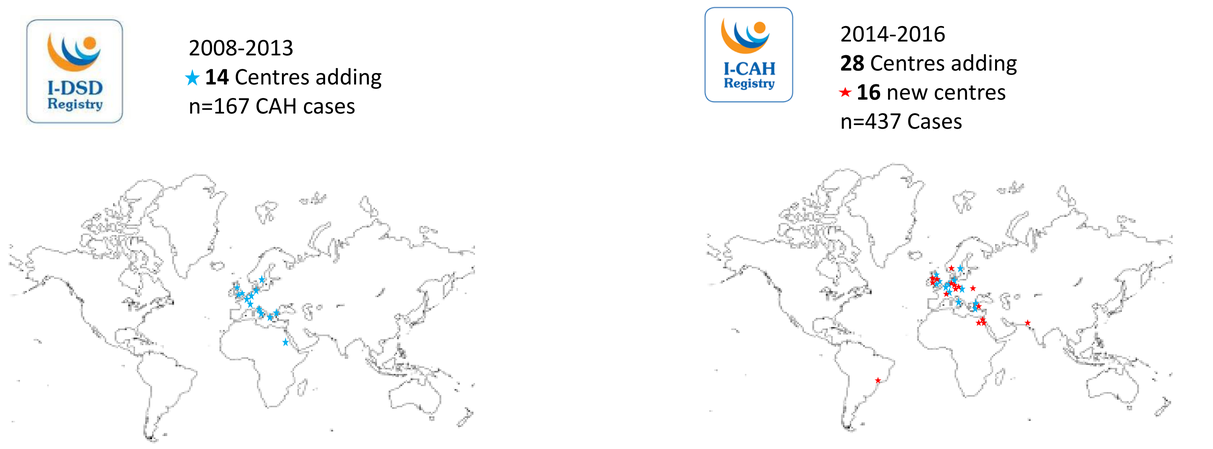

Figure1: Comparison between the number and distribution of centres adding CAH cases before and after the creation of the I-CAH Registry

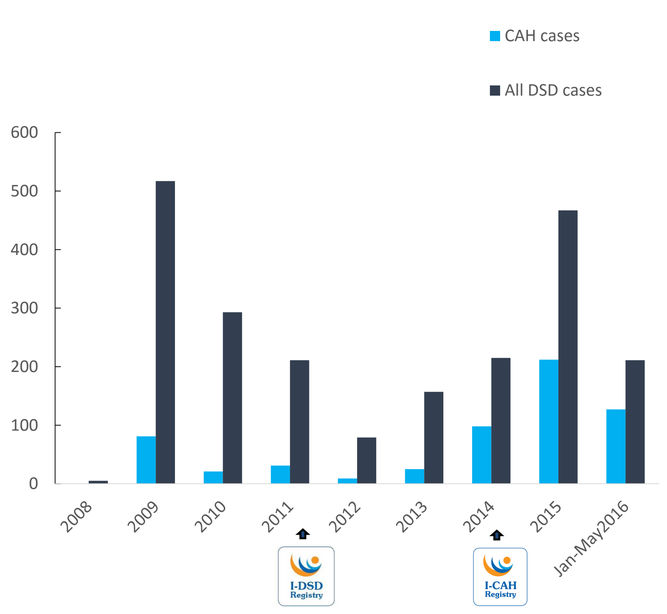

Figure2: The rate of addition of CAH cases per year compared to the rate of addition of all DSD cases

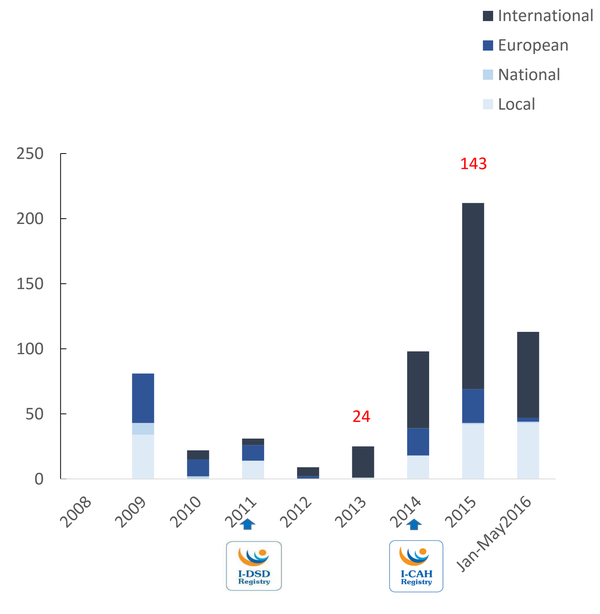

Figure3: The evolution of the level of sharing of data in CAH cases

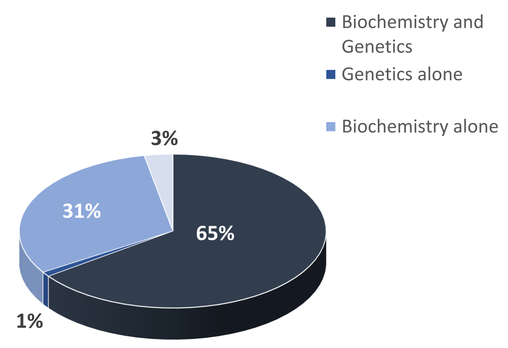

Figure4: The distribution of CAH cases depending on the basis of Diagnosis

Basis of Diagnosis for CAH cases	Genetic and Biochemistry n= 109	Biochemistry alone n=53	p value
Median year of birth	2006 (1964-2015)	2001(1967-2014)	p=0.0015
Age at first presentation	1m(1m-48yrs) >2yrs: n=14 (13%)	3m(1m-18yrs) >2yrs: n=12(22%)	p=0.0054
Median upload year	2014(2009-2016)	2011(2009-2016)	p=0.0013
Centres adding CAH cases	n=18 E=15 (85%) NE=3(15%)	n=13 E=7 (54%) NE=6 (46%)	

Table: Characteristics of cases confirmed genetically compered to cases confirmed by biochemistry only

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