Factors affecting loss to follow-up in children and adolescents with chronic endocrine conditions: a regional cohort study

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INTRODUCTION

➢Most patients with endocrine diseases diagnosed during childhood require long-term continuity of care.

➢A lack of regular medical follow-up visits may be associated with poorer long-term health outcomes, with greater risks of morbidity and mortality.

➢The importance and challenges of the transition from pediatric to adult healthcare are well recognized but few studies have considered loss to follow-up (LTFU) during pediatric care, despite the importance of adherence to medical care in a context of successful clinical management for health, growth and development in children.

AIM OF THE STUDY

To investigate the prevalence of LTFU during pediatric care, in patients with chronic endocrine diseases and to identify risk factors associated with LTFU.

PATIENTS AND METHODS

➢ This **observational cohort study** included all patients :
- < 16 years at the beginning of the study (January 2007)
- with chronic endocrine diseases
- ≥ 1 medical visit between January 2007 and June 2014 (study end point : December 2016)

➢ **LTFU** = a lack of attendance at clinical visits for ≥ 2 years, for unknown reasons

➢ **Chronic endocrine diseases in this study:**

❖ **Pituitary**
- Isolated Growth Hormone Deficiency (IGHD)
- Multiple Pituitary Insufficiency (MPHD)
- Congenital hypogonadotropic hypogonadism

❖ **Thyroid**
- Congenital hypothyroidism
- Graves' disease

❖ **Turner syndrome**

❖ **Idiopathic 46,XY Disorders of Sex Development (DSD)**

❖ **Non-idiopathic DSD**

➢ **Congenital hypogonadotropic hypogonadism or DSD** :
- Such frequent clinical care is unnecessary during the prepubertal period after initial management.
- LTFU was defined as an
  - absence of clinical visits after the age of 13 years in girls and 14 years of boys
  - not returning to the clinic after the age of 15 years for girls and 16 years for boys

RESULTS

LTFU was recorded for 154 of the 1067 patients included (14%). Median age at diagnosis was 5.8 (0.3-11.8) vs. 1.2 (0.0-6.9) years, and age at last visit was 14.1 (9.7-16.1) vs. 11.7 (6.1-15.8) years, for the LTFU and no LTFU groups, respectively.

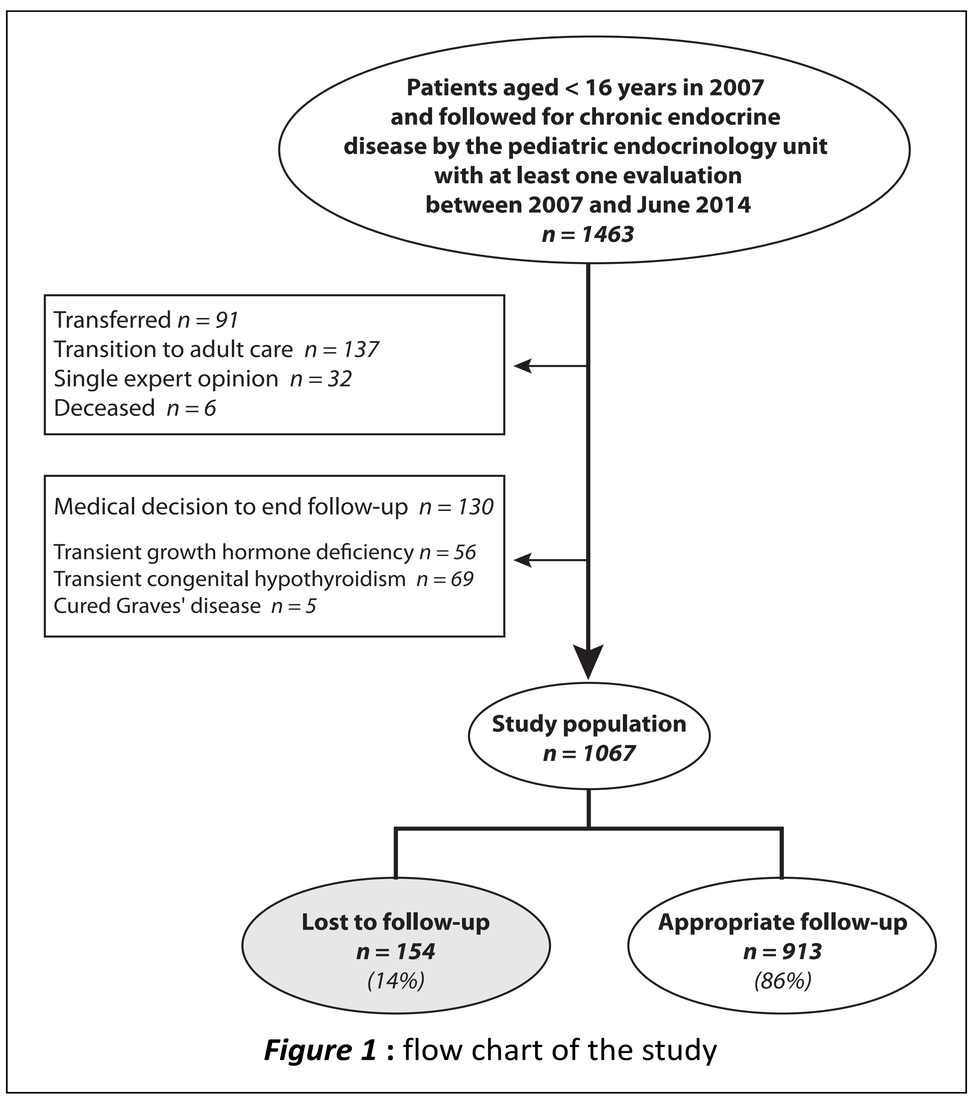

Figure 1 **:** flow chart of the study

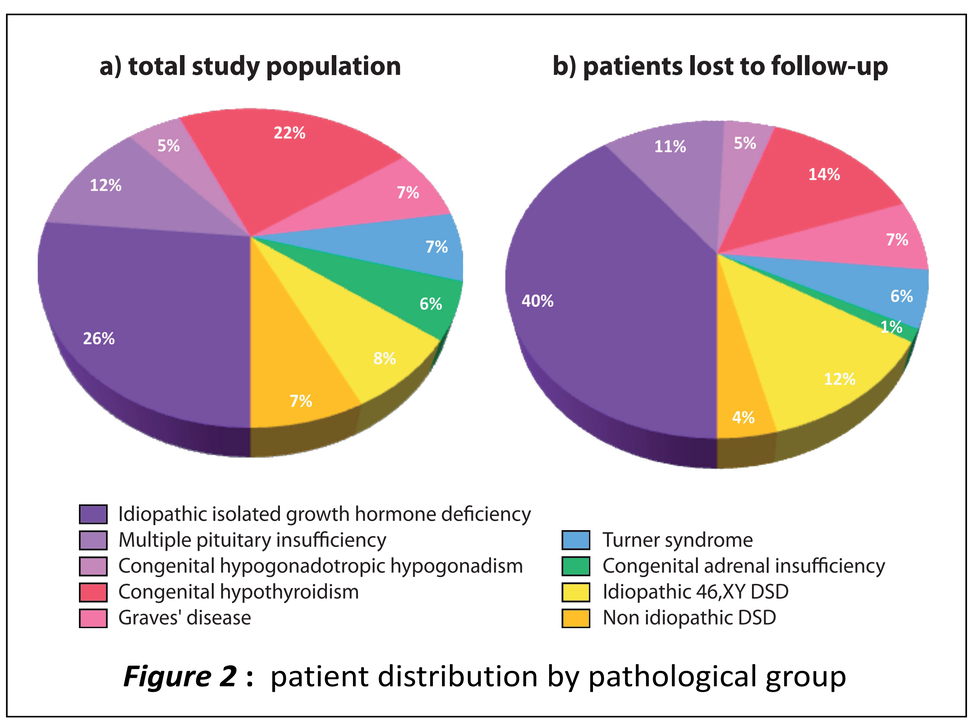

Figure 2 **:** patient distribution by pathological group

Table 1 : Uni- and multivariate models analyzing loss to follow-up during the pediatric period for patients with endocrine conditions

	Univariate analysis		Multivariate analysis	
	OR [95% CI]	*P*-value	OR [95% CI]	*P*-value
Sex (M/F)	0.88 [0.62 ; 1.24]	0.47	ND	ND
Age at diagnosis (years); median (Q1 ; Q3)	1.10 [1.07 ; 1.14]	**<0.0001**	1.18 [1.12 ; 1.24]	**<0.0001**
Duration of follow-up (ref < 2 years)				
2-4 years	0.36 [0.21 ; 0.62]	**0.0002**	ns	ns
> 4 years	0.28 [0.18 ; 0.43]	**<0.0001**	ns	ns
Current age at study end point (years) (ref < 15 years)				
≥ 15 years	6.41 [4.28 ; 9.61]	**<0.0001**	ND	ND
Diagnosis period (ref ≥2006)				
<2006	2.54 [1.79 ; 3.62]	**<0.0001**	4.80 [3.00 ; 7.66]	**<0.0001**
Prescription of hormonal treatment during last visit (ref no)				
Yes	0.30 [0.21 ; 0.43]	**<0.0001**	ND	ND
Number of medical evaluations during the last 3 years	0,78 [0,72 ; 0,84]	**<0.0001**	0.72 [0.65-0.8]	**<0.0001**
Country of birth (ref: another country)				
France	1.46 [0.73 ; 2.91]	0,29	ND	ND
National health insurance system (ref: standard regime)				
Precarious regime (AME, CMU and/or CMUc)	1.58 [1.01 ; 2.45]	**0.04**	1.79[1.1 ; 2.89]	**0,02**
Subgoups based on pathological condition (ref: congenital adrenal insufficiency)				
Isolated growth hormone deficiency (IGHD)	8.11 [1.93 ; 34.12]	**0.004**	5.24 [1,13 ; 24.37]	**0.03**
Multiple pituitary insufficiency (MPHD)	4.56 [1.02 ; 20.41]	**0.05**	2.92 [0.59 ; 14.42]	0.19
Congenital hypogonadotropic hypogonadism	4.49 [0.89 ; 22.64]	0.07	1.17 [0.2 ; 6.74]	0.86
Congenital hypothyroidism	3.08 [0.70 ; 13.46]	0.14	2.13 [0.45 ; 10.05]	0.34
Graves' disease	4.84 [1.03 ; 22.74]	**0.05**	2.44 [0.46 ; 13.02]	0.30
Turner syndrome	4.08 [0.85 ; 19.67]	0.08	1.75 [0.33 ; 9.23]	0.51
Idiopathic 46,XY DSD	9.04 [2.02 ; 40.51]	**0.004**	4.27 [0.86 ; 21.31]	0.08
Non-idiopathic DSD	2.49 [0.48 ; 12.81]	0.27	0.86 [0.15 ; 4.86]	0.87

Results not significant for : sex, country of birth and the other subgroups based on pathological condition

In multivariate analysis, the risk of LTFU increased with **age at diagnosis** (OR 1.18; 95%CI: 1.12-1.24), and was higher for **patients diagnosed before 2006** (vs. after 2006) (OR 4.80; 3.00-7.66), with **fewer visits in the last three years** (OR 0.72;0.65-0.80);(*p*<0.0001), and a **lower health insurance classification** (OR 1.79;1.10-2.89;*p*=0.02).

The risk of LTFU was higher for patients with **isolated GH deficiency** than for those with other endocrine conditions, such as multiple pituitary deficiencies, hypogonadotropic hypogonadism, thyroid, Turner syndrome, adrenal or gonadal disorders (OR 5.24;1.13-24.37; *p*=0.03).

SUMMARY

❖ **14% LTFU**

❖ **5 risks factors** identified :
- Greater age at diagnosis
- Diagnosis before 2006 → creation of the reference centre with a nurse dedicated to therapeutic education
- Lower frequency of medical visits
- Lower socio-economic status reflected by their type of health insurance
- Isolated GH deficiency

CONCLUSION

These original findings have important clinical implications for patient management, as they highlight the need for careful monitoring for the early recognition of features associated with a risk of LTFU in patients with chronic endocrine disorders of childhood onset. This would potentially improve their long-term outcomes.

Future studies should explore target interventions for improving adherence to medical care and improvements in healthcare organization during the pediatric period.

58ESPE RFC3-002
Multisystem endocrine disorders
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Poster presented at: ESPE 2019 VIENNA
PosterSessionOnline.com