CLINICAL FEATURES AND ASSESSMENT OF THE PATHWAY-CARE PROPOSED BY ISPED-GSα STUDY GROUP IN A PEDIATRIC ITALIAN COHORT WITH PSEUDOHYPOPARATHYROIDISM

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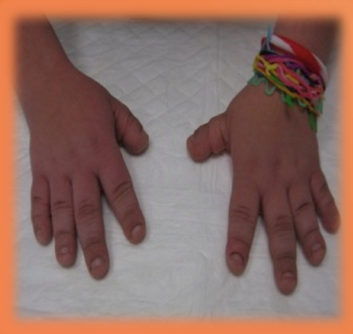
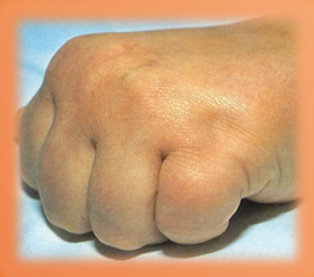
BACKGROUND AND OBJECTIVES

Pseudohypoparathyroidism (PHP) **refers to a heterogeneous group of rare endocrine disorders caused by genetic or epigenetic abnormalities affecting the GNAS locus. It is mainly characterized by resistance to PTH and TSH and a complete or partial Albright Hereditary Osteodistrophy (AHO) phenotype. Few data so far exist on GHRH and LH/FSH resistance, calcitonin resistance and glucose-lipid metabolism involvement, as well as on neurocognitive aspects. The recently published healthcare-pathway proposed by the Italian Society of Pediatric Endocrinology and Diabetology (ISPED) has standardized the clinical approach to these patients.**
The present aim is to assess the adherence to the healthcare-pathway of the main Italian Pediatric Endocrine Centres, outlining the current state of follow-up and to obtain preliminary data on prevalence, correlation and evolution of PHP features, above all the less studied ones.





METHODS

23 PHP patients followed by 5 Italian Pediatric Endocrine Centres were enrolled, 14 of which have a genetic mutation in the GNAS gene, while the other 9 display a wild-type sequence of the gene. A common standardized chart has allowed to assess the adhesion to the healthcare pathway; in particular, data on auxological variables calcium-phosphorus metabolism, thyroid function, FSH/LH levels, calcitonin, glucose-lipid metabolism, subcutaneous ossifications, neurocognitive development and general health have been collected.

RESULTS

Current state of follow up

An improvement in the utilization of the shared protocol has emerged, above all in the less explored fields of the disease, such as pregnancy and delivery course, calcitonin, FT4 at control and GH levels, glucose-lipid metabolism and neurocognitive development.

OUTCOME	DATA COLLECTION	
	partial	absent
Pregnancy and delivery course	57%	4%
Ca-P metabolism (Calcitonin)	78%	-
Thyroid function (FT4 at control)	57%	4%
GH levels and growth	48%	4%
Glucose-lipid metabolism	35%	22%
Neurocognitive development	44%	4%

Auxological data

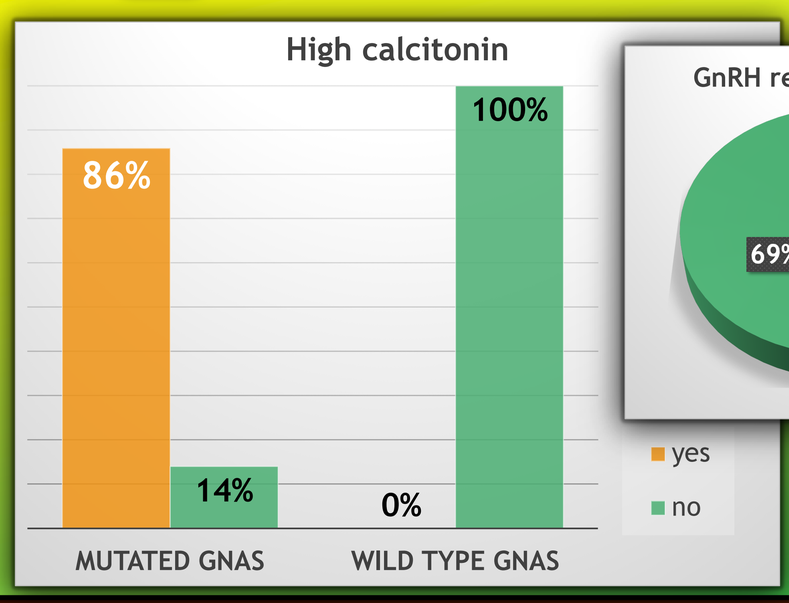
The average age at diagnosis in patients with mutated GNAS gene is lower than in patients with WT gene (5.18 vs 9.25 y.o., p=0.049). Pregnancy and/or delivery complications and SGA were reported in 68 and 18%, respectively; overweight or obesity (average BMI 23.32, +1.44SDS) and height <-2SDS (average 139.8 cm, -1.12SDS) in 61% and 24%, respectively. in 4/23 patients the GH-stimulation test has confirmed a resistance eligible for rhGH-therapy, whereas in 35% IGF1 was <0SDS. Bone age was advanced in 69% of cases.

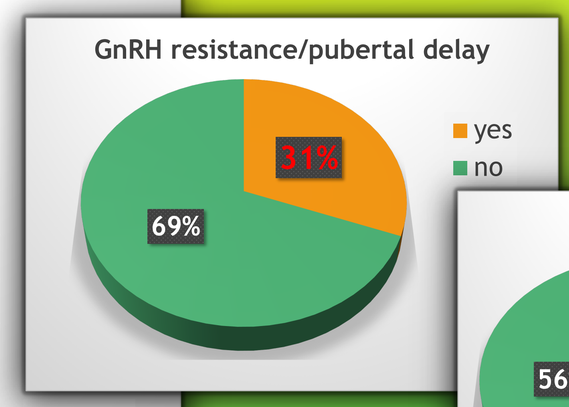
Biochemical parameters

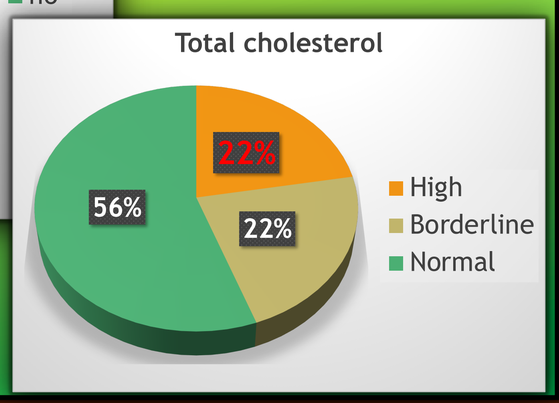
At diagnosis, 91% of patients showed increased PTH, 48% hypocalcemia and 67% hyperphosphatemia; after 1,25OH-VitD treatment alone or associated with Calcium, the prevalence decreased to 76%, 0% and 33% respectively. Bone mineralization was appropriate in all patients. A negative correlation was observed between PTH and Calcium levels (r Pearson=-0.66).
At diagnosis, clinical hypothyroidism was present in 61% of patients; after substitutive therapy, in 23% as subclinical form. At diagnosis, the mutated subjects displayed TSH higher mean value (p=0.04), lower FT4 (p=0.02) than WT patients; at early puberty height was lower in the first group of patients (p=0.02).

Focus on less studied PHP features

A FSH/LH resistance has been found in 31% of the whole cohort and calcitonin increased levels in 55% of patients, all with mutated gene. Glucose metabolism was normal in 95% of patients, while 22% showed hypercholesterolemia, 11% hypertriglyceridemia and 78% HDL-C reduced levels. Finally, subcutaneous ossifications have been described in 32% of patients, delayed neurocognitive development in 63%, psychological support needs in 22%.







CONCLUSIONS

ISPED healthcare-pathway hasn't been completely adopted yet, but it is confirmed to be a valid instrument to conform the clinical approach to PHP patients, with the dual aim to guarantee the best management to all patients and to allow homogeneous data collection, useful for a disease with heterogeneous and complex clinical manifestations, such is Pseudohypoparathyroidism.

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NO conflict of interest

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