

Clinical features and body mineral density in Italian patients with rapid onset obesity with hypoventilation, hypothalamic dysfunction, autonomic dysregulation and neural tumor (ROHHADNET): a single center observational study.

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Background and Aim

ROHHAD (rapid onset obesity with hypoventilation, hypothalamic dysfunction, autonomic dysregulation) syndrome is a rare and underdiagnosed disease with high morbidity and high mortality rate. When a neural crest tumor (NET) is detected (56% of patients) the acronym used is ROHHADNET. The aim of this study is to analyze the relationship between clinical variables, hypothalamic-pituitary disorders, DXA parameters and neural tumors, in ROHHAD and ROHHADNET patients.

Subjects and Methods

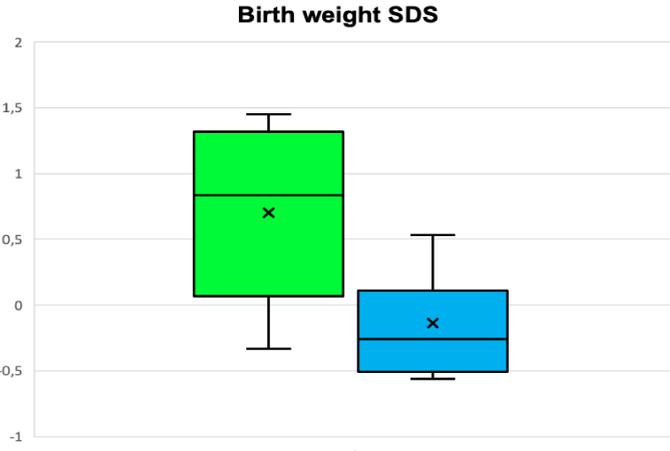
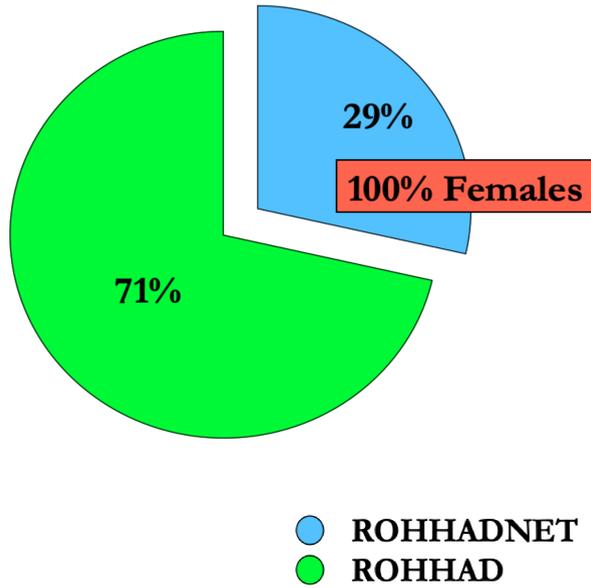
We included individuals with ROHHAD and ROHHADNET, who were followed at our centre (Pediatric Endocrine Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy) between January 2008 and December 2020 (median follow up 7.82 years, 4.12-8.80 y). They were selected by clinical criteria, after excluding Prader-Willi Syndrome and Congenital Central Hypoventilation Syndrome. Medical history, anthropometric, hormonal and densitometric data were collected for the two groups of patients (ROHHAD and ROHHADNET) and analyzed.

Results

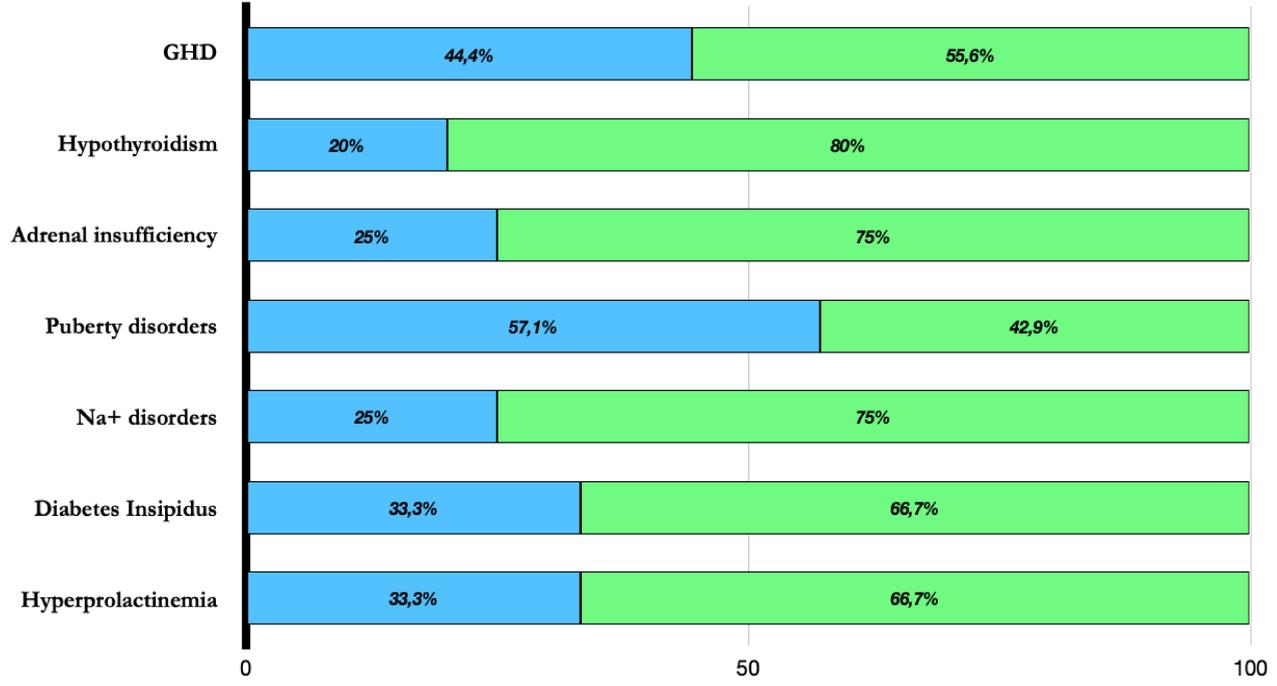
In our cohort of 14 patients (9 females, 64,3%), NET are reported in 4 females (28,5%). Median age at rapid weight gain onset is 3 years in both groups (2.5 – 3 vs 1.5 – 4). Median BMI SDS at diagnosis is +4.13 vs +4.6. Seven patients have pubertal disorder (either precocious puberty or central hypogonadism), 4 patients with NET (57,1%) and 3 without NET (42,9%) (p=0.2). Nine patients have GHD, 4 with NET (44,4%) and 5 without NET (p=0.22). Ten patients have central hypothyroidism, 2 with NET (20%) and 8 without NET (p=0.52). Eight patients have adrenal insufficiency, 2 with NET (25%) and 6 without NET (p =1.00). Prolactin level is elevated in all patients with NET, and 8 patients without NET. Five patients have strabismus, 3 patients with NET (60%), and 2 without NET (p =0.1). Nine patients have autonomic dysfunction, 1 with NET (11,1%), and 8 without NET (p =0.1). Back to data from birth, there is no difference in standardized birth length between the two groups, while patients with NET show a lower median birth weight SDS (-0,26 vs 0,84, p=0.06). Regarding DXA parameters, there is no difference in BMD SDS total body between ROHHAD and ROHHADNET patients, while ROHHADNET show a higher BMD SDS L1-L4 (1.55 vs 0.7) (p =0.06).

Conclusions

Our patients with ROHHAD who developed NET are females (100%), they tend to have a lower birth weight, higher BMD SDS L1-L4, and greater incidence of strabismus and autonomic dysfunction. None of these associations are significant because of the low number of enrolled patients. Multicentric cohorts need to be analyzed in order to better understand the clinical characteristics of this rare and severe disease.



Prevalence of neural tumors (NETs) in ROHHAD patients with hypothalamic-pituitary disorders



Association between DXA parameters and neural tumors (NETs)

	NET Yes (n=4)	NET No (n=10)	P value
BMD-z score L1-L4	1.55 (0.45 - 2.3)	0.7 (-0.7 - 0.9) [n=9]	0.06
BMD-z score Total Body Less Head	1.25 (0.55 - 2)	0.4 (-0.55 - 1.35) [n=8]	0.27
BMD-z score Total Body	1.1 (0.95 - 1.85)	0.6 (-0.4 - 1.5) [n=9]	0.40
Android/Gynoid Ratio	1.05 (0.95 - 1.12)	0.97 (0.93 - 1.01)	0.29
Truncal Fat mass / Total Fat mass	0.52 (0.48 - 0.54)	0.48 (0.47 - 0.51)	0.47
Percentage of Fat mass	50.36 (42.63 - 53.78)	46.81 (43.99 - 51.33)	0.72
Percentage of Fat Free mass	44.77 (40.68 - 49.79)	44.33 (40.84 - 48.25)	0.94

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