“NATIONWIDE HYPOPHOSPHATEMIC RICKETS COHORT STUDY”

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Aim: Hypophosphatemic rickets (HR) is a rare renal phosphate wasting disorder commonly related to X-linked form, caused by *PHEX* mutations and it treatment and follow-up is challenging due to imperfect treatment options. We aimed to present a nationwide data on HR with initial and follow-up data on the patients presented to the pediatric endocrinology clinics

Method: CEDD-NET Data were used

Inclusion criterias:

- Diagnosed between 0 to18 years of age
- Hypophosphatemia
- Renal phosphate wasting

Exclusion criterias:

- Calciopenic Rickets

Results:

From 24 centers, 158 patients, before the age of 18 years, were included in the study data. Genetic analysis (n:75) showed PHEX mutation in 80%. The mean follow-up period was 6.7±2.4 years.

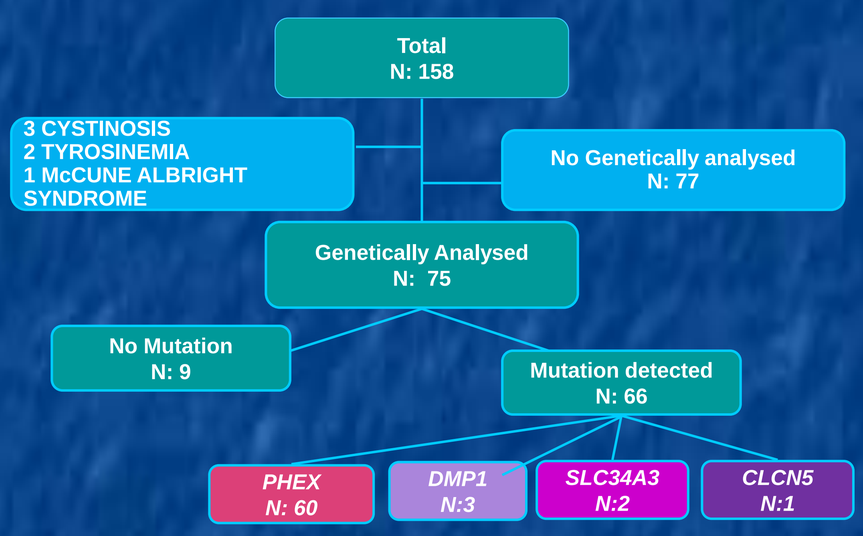
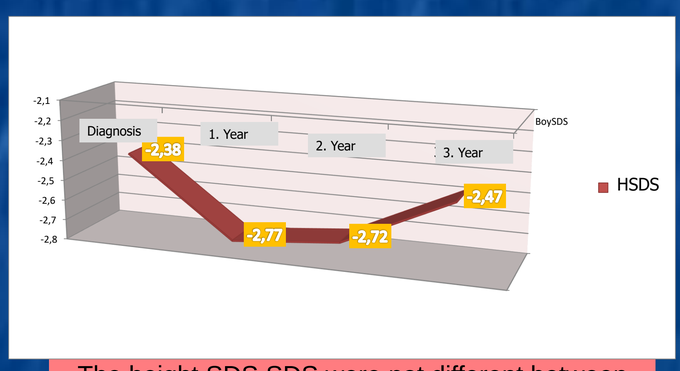


Table 1: Characteristics of cases

Characteristics	
Age of diagnosis (year)	5.25 ± 3.84
Height SDS	-2.41 ± 1.34
Puberty	Pubertal → 16 Prepubertal → 138
Begining of Symptoms (month)	22.77 ± 23.55
Start of walking (month)	15,67 ± 3.82
Positive family history (n, %)	79 (50,6%)

In follow-up: First 3 years treatment response (N:91) of patients, mild increase in P (from 2.6±0.6 to 2.7±0.6, 2.8±0.7 and 2.8±0.7 mg/dl), decrease in ALP (from 786±522 to 627±449, 561±319 and 546±327 U/L) and, elevation in PTH levels (from 68±48 to 84±77, 79±66 and 93±99 pg/ml) had been detected (from intitial to 1st, 2nd and 3rd year, respectively) .



The height SDS SDS were not different between the years of treatment!

36% of the patients showed complete or partial improvement in leg deformities

Table 2: Doses of treatment and growth characteristics of improved and unimproved groups

	Phosphate dose (mg/kg)			Calcitriol dose (ng/kg)			Height SDS		
	Impr.	Not Impr.	*P values*	Impr.	Not impr.	*P values*	Impr.	Not impr.	*P values*
At Diagnosis	61,3	60,8	*0,478*	33,15	26,9	*0,085*	**-2,07**	**-2,57**	***0,039***
1. Year	64,8	62,1	*0,39*	**32**	**24,9**	***0,02***	**-2,04**	**-2,67**	***0,014***
2. Year	59,9	56,5	*0,32*	28,1	26,3	*0,26*	**-2,07**	**-2,71**	***0,009***
3. Year	65,4	54,69	*0,08*	**26,9**	**22,06**	***0,033***	**-1,92**	**-2,8**	***<0,001***

Imp: Improved in leg deformitese, Not Impr: Not improved in leg deformities

Table 3: Laboratory characteristics of improved and unimproved groups

	Phosphate level (mg/dl)			Calcium level (mg/dl)			ALP level (U/L)			PTH level		
	Impr.	No Impr.	*P values*	Impr.	Not impr.	*P values*	Impr.	Not impr.	*P values*	Impr.	Not impr.	*P values*
At Diagnosis	2,58	2,6	*0,24*	9,3	9,46	*0,28*	**528**	**688**	***0,01***	60,9	68,6	*0,47*
1. Year	**2,9**	**2,63**	***0,01***	9,1	9,48	*0,22*	**433,5**	**537,4**	***0,009***	92	82	*0,38*
2. Year	**3,02**	**2,72**	***0,028***	9,4	9,57	*0,38*	**573**	**503,8**	***0,014***	76,5	84,7	*0,18*
3. Year	2,6	2,73	*0,08*	9,25	9,55	*0,22*	612	505,2	*0,058*	109	83,6	*0,12*

Nephrocalcinosis (NC) was developed 17% of patients

Table 4: Treatment characteristics of Patients according to development of nephrocalcinosis

	Phosphate dose (mg/kg)			Calcitriol dose (ng/kg)		
	NC (+)	NC (-)	*P values*	NC (+)	NC (-)	*P values*
At Diagnosis	**89.9**	**55,95**	***0,003***	**62,37**	**27,92**	***0,006***
1. Year	74,31	60,61	*0,13*	**34,9**	**26,4**	***0,04***
2. Year	**71,93**	**54,69**	***0,033***	26,43	27,17	*0,48*
3. Year	69,4	56,76	*0,096*	**18,66**	**25,16**	***0,035***

Table 5: Laboratory characteristics of Patients according to development of nephrocalcinosis

	Phosphate level (mg/dl)			Calcium level (mg/dl)			ALP level (U/L)			PTH level		
	NC (+)	NC (-)	*P values*	NC (+)	NC (-)	*P values*	NC (+)	NC (-)	*P*	NC (+)	NC (-)	*P values*
At diagnosis	2,47	2,59	*0,209*	9,42	9,5	*0,25*	861	769,9	*0,29*	48,6	72,7	*0,06*
1. Year	2,92	2,71	*0,114*	9,29	9,48	*0,11*	606,9	631,8	*0,4*	114,1	78,5	*0,069*
2. Year	2,95	2,81	*0,24*	9,54	9,56	*0,42*	571,5	559,7	*0,44*	85,4	78,4	*0,36*
3. Year	2,75	2,82	*0,36*	9,5	9,6	*0,21*	571,8	541,1	*0,37*	154,	78,2	*0,002*

Conclusion: HR treatment and follow-up is challenging and higher calcitriol doses could improve bone deformities. However, higher treatment doses leading nephrocalcinosis without any change in serum levels, suggesting given higher doses lead higher phoshaturia probably through the stimulation FGF23. Safer and more efficacious therapies are needed.