REAL-LIFE PRACTICE IN THE MANAGEMENT OF FABRY DISEASE – PRELIMINARY RESULTS

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INTRODUCTION

- Fabry disease is an X-linked lysosomal storage disease caused by deficient activity of lysosomal enzyme α – galactosidase A.
- It leads to deposition of glycosphingolipids, mainly globotriaosylceramide, resulting in varying degrees of organ dysfunction, such as chronic kidney disease.
- Fabry nephropathy, a cardinal finding in Fabry disease, is characterized by glomerular filtration rate decline, albuminuria, and tubular dysfunction.
- The expected decline in glomerular filtration rate (GFR) in Fabry nephropathy varies according to gender and initial renal function, ranging from 0.9 to 3.0 ml/min/1.73m^2 ,in patients with GFR> 60 ml/min /1.73m^2, to 2.1 to 6.8 ml/min/1.73m^2 per year for GFR below this value.

OBJECTIVE

The aim of the study was to evaluate the clinical evolution of Fabry nephropathy in a real-world medical practice condition.

METHODS

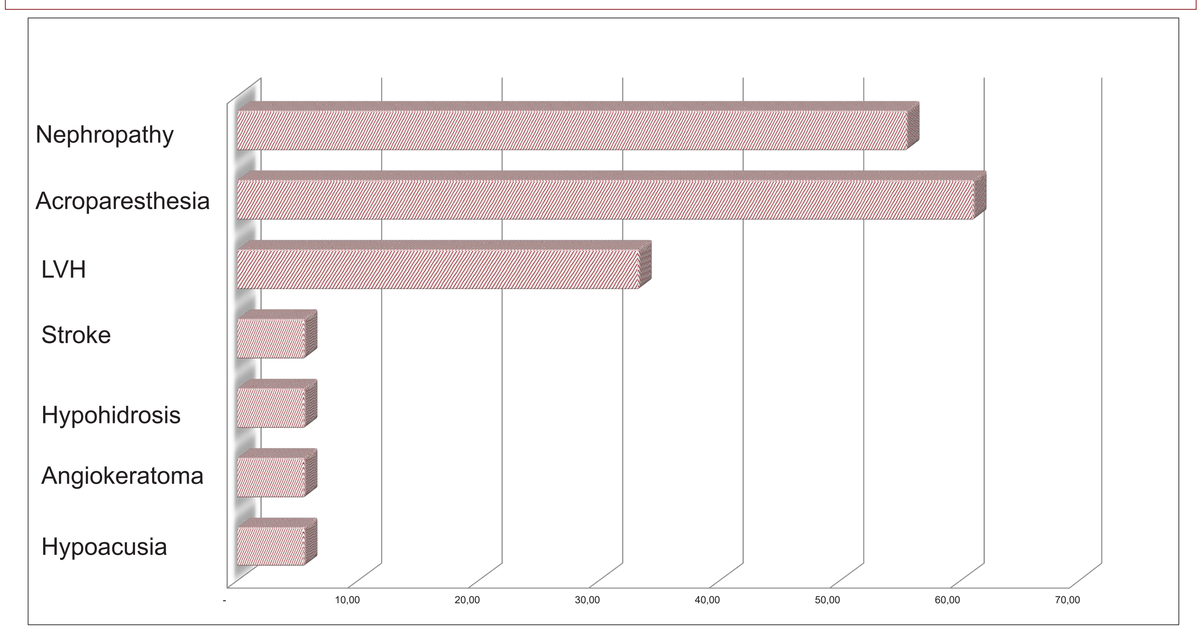
- This is a retrospective study that evaluated Fabry disease patients followed in the outpatient Clinic Center for Fabry Disease in Tapejara - Brazil.
- Inclusion criteria:
  - Measurement of serum creatinine and proteinuria prior to enzyme replacement therapy (ERT) initiation.
- Glomerular filtration rate was estimated based on the CKD-EPI formula.
- Renal function reduction was defined as a rise in serum creatinine > 25% from baseline.
- Clinical and laboratory data were collected from medical records.

RESULTS

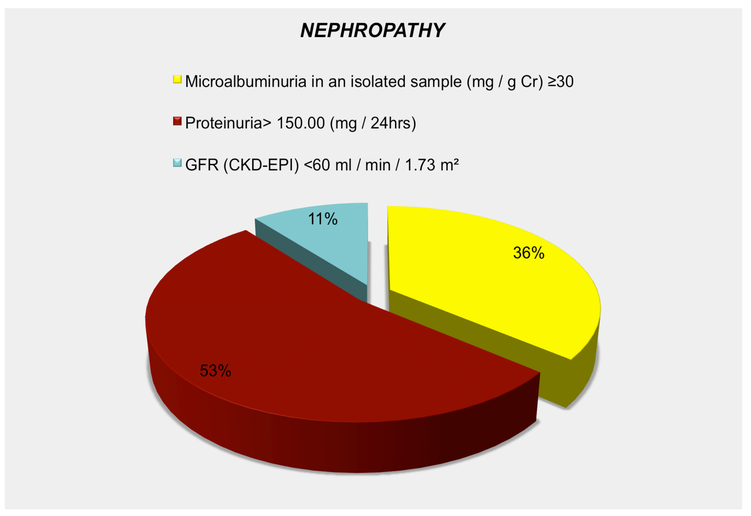
BASELINE RENAL MANIFESTATIONS AND MUTATION PER PATIENT

patient number	gender	age (years)	mutation	creatinine (mg/dl)	eGFR (mL/min/1.73 m²)	proteinuria (mg/24 hours)	albuminuria (mg/g Cr)
1	F	57	P.Y365X	0.90	71.00	93.00	11.00
2	F	21	W47X	0.60	129.40	---	---
3	F	16	W47X	0.72	124.00	85.84	25.60
4	F	19	P. Y365X	0.70	125.60	---	---
5	F	28	P. Y365X	0.70	110	---	---
6	F	40	P. Y365X	0.90	80.00	144.80	22.90
7	F	45	P. Y365X	1.30	49.50	2500.00	1766.00
8	F	36	P. Y365X	1.01	71.60	33.10	---
9	F	23	W47X	0.80	103.90	123.80	6.20
10	F	15	P. Y365X	1.12	73.20	192.00	19.00
11	F	63	P. Y365X	0.66	94.00	---	---
12	F	21	P. Y365X	0.60	130.30	467.00	212.00
13	M	33	P.W204X	0.76	119.90	440.00	---
14	F	22	P. Y365X	0.80	104.60	190.00	25.10
15	F	16	P. Y365X	0.90	94.70	60.00	12.18
16	F	55	P. Y365X	1.09	57.10	72.00	13.00
17	F	45	P. Y365X	0.80	89.00	203.00	87.90
18	F	25	P. Y365X	0.50	134.50	350.00	190.00

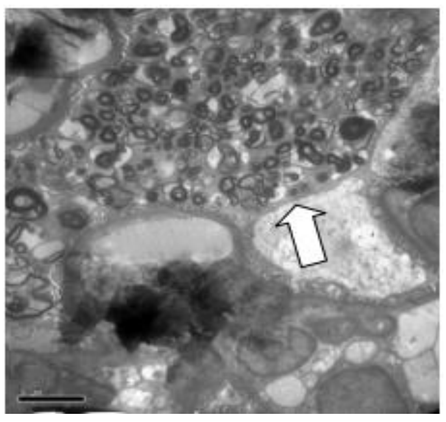
CLINICAL MANIFESTATIONS OF FABRY DISEASE



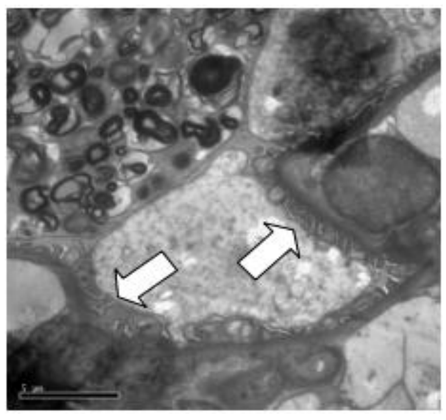
RESULTS



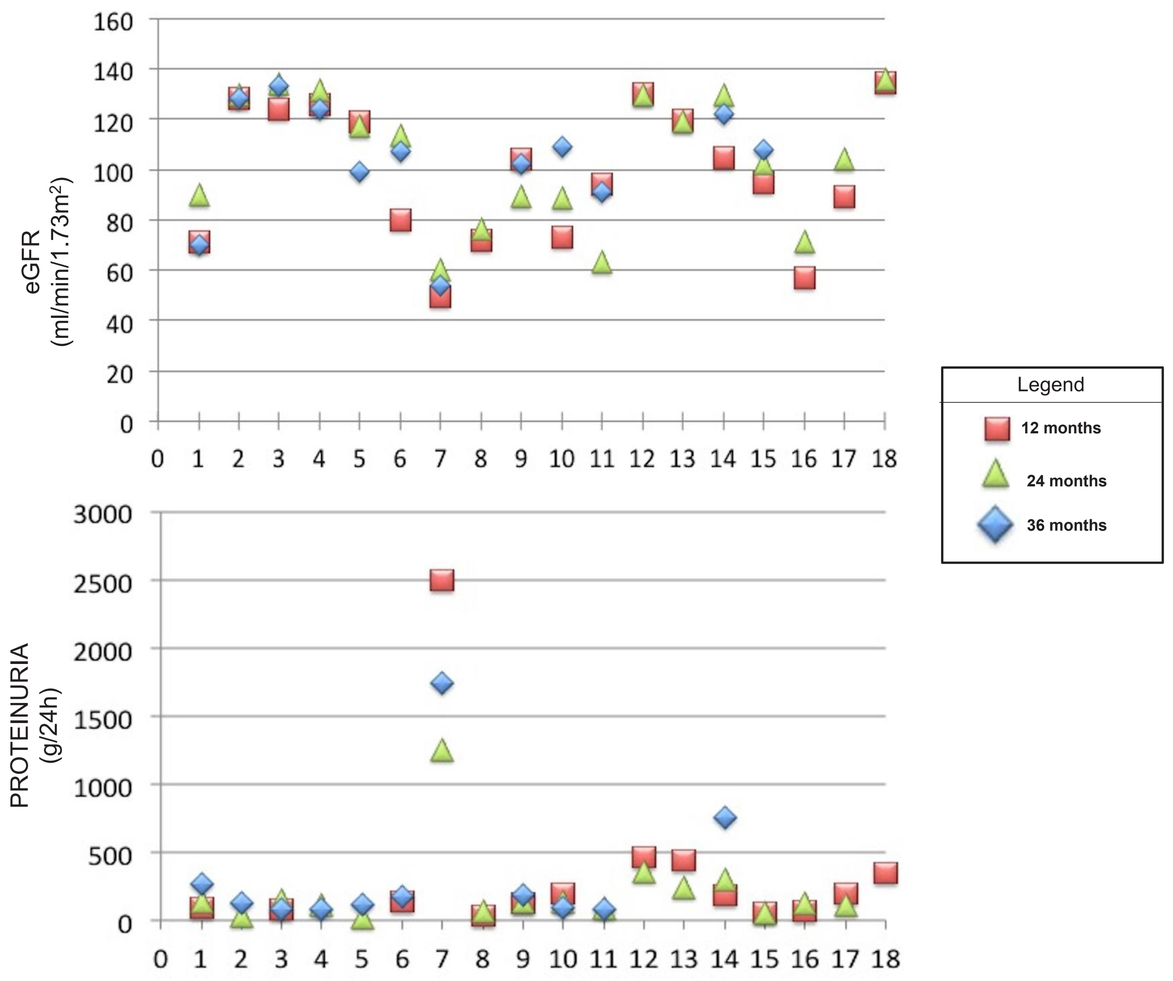
ELECTRON MICROSCOPY FINDINGS OF KIDNEY BIOPSY BEFORE ERT FROM PATIENT no. 10



Regular capillary loops, with podocytes degenerative changes (Arrow)
(Electron Microscopy- 3000X)



Podocytes with degenerative changes and retraction of pedicels with intracytoplasmic "myeloid bodies"(arrows)
(Electron Microscopy - 6000X)



CONCLUSIONS

- ✓ Our preliminary findings give support to the concept that ERT combined with renin-angiotensin system blockade is an effective strategy to prevent progression of Fabry nephropathy for up to 36 months. The study design prevent us from evaluating the individual effect of ERT.
- ✓ Heterozigous Fabry women should not be neglected. They may present significant disease burden, including renal and cardiac involvement, and must be treated accordingly.
- ✓ Studies based on clinical practice can be interesting and more economically viable alternatives than randomized clinical trials, particularly in the setting of rare diseases for which recruitment and inclusion of patients is extremely difficult.

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