Cystinosis Registry of India: Data Analysis of Patients with Cystinosis (2023)

Dear Editor,

Cystinosis is a rare autosomal recessive lysosomal storage disorder caused by mutations in the *CTNS* gene on chromosome 17p13. The *CTNS* gene encodes the lysosomal cystine transporter cystinosin. Defective transportation from the lysosomes results in the accumulation of cystine in the cytoplasm of cells, which in turn leads to apoptosis and progressive organ dysfunction. Diagnosis is confirmed by finding elevated cystine levels in leukocytes (5–23 nmol hemicystine/mg protein, normal level ≤0.2 nmol hemicystine/mg protein) and genetic testing for mutations of the *CTNS* gene.

Cysteamine treatment results in the production of cysteine and cysteine–cysteamine molecules from cystine, which are transported from lysosomes by alternative transporters. This results in the depletion of cystine in the cells, thereby reducing the progression of disease. Cysteamine is available as an immediate-release oral formulation that needs to be given every six hours. Cysteamine eye drops are available, but it should be administered every two to four hours. Such a rigorous schedule is challenging to maintain for a lifetime. Kidney transplantation is the treatment of choice in end-stage kidney disease, and if leukocyte cystine levels are maintained within the acceptable range (0.5–1 nmol hemicystine/mg protein), cystinosis does not recur in the graft.[1]

There have been a few reports of cystinosis from India.[2–4] India and other developing countries face several challenges in managing this disease. A study compared the management strategies of developing nations with that of developed nations and found that 7% of patients died at a mean age of five years compared to none in developed nations and a higher number of patients reached end-stage kidney disease earlier (53.2 vs. 37.9%, P = 0.03, 8 vs. 10 years, P = 0.0008).[5] Kidney transplantation in a child with cystinosis from India was first reported in 2010.[4] The Cystinosis Foundation of India was launched in 2012 by Sapiens Health Foundation, a non-governmental organization.

A report on the patients registered with the Foundation was first published in 2016.[4] A total of 42 patients were registered until the end of 2022 [Table 1]. Twenty eight children were on follow-up. Eight children were less than two years of age at diagnosis. The mean age was 6.5 years (range: 1–21 years, median: 5.5 years). There were 29 boys and 13 girls. Growth retardation was the most common presentation in 39 children. Fanconi syndrome was noted in 35 children. Renal impairment was noted in 34 of them, and 2 children were on continuous ambulatory peritoneal dialysis. Six children underwent kidney transplantation and two of them developed graft failure. Siblings were affected in 14 children. A total of 16 patients were born from, consanguineous parents. Corneal crystals was the most common finding in 38 children. Hypothyroidism was also present in 22 children. Common complications included recurrent episodes of dehydration (that required intravenous fluids), severe hypokalemia, hypocalcemia, hypophosphatemia, metabolic acidosis, and recurrent infections. Cysteamine was started in 25 children. The mean duration of follow-up was 43.81 months (range: 1–129 months). Twelve children died during the follow-up. Since most of the patients registered with the foundation were managed by various nephrologists scattered throughout the country, the exact cause of death was unknown. Cystinosis Foundation of India has helped patients with the paperwork involved when importing cysteamine (not available in India) and raising funds to import it. The Drug Controller General of India provides special permission from individual patients to import the drug. Orphan Europe, now known as Recordati Rare Diseases Foundation, has almost 30 years of experience in bringing orphan drugs to the market for rare diseases. The drug is sent by courier after money is remitted, from the Recordati Rare Diseases Foundation, which needs to be cleared by the Customs of India before it can finally reach the patient. A month's supply of the drug costs approximately ₹15,000; this cost is not covered by insurance. Treatment needs to be lifelong, which imposes a significant financial burden.

Patient registries are key to gathering important clinical data that can achieve a sufficient sample size to conduct research and help provide evidence that orphan drugs work.

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Nil.

Table 1: Clinical data of patients in the cystinosis registry of India

Age at diagnosis (years)	Gender	Affected sibling	Consanguinity	Clinical features	Cysteamine	Follow-up (months)
12	M	Yes	Yes	GR, H, CC, FS, CKD, RTR	Yes	Yes, 129
7	M	Yes	Yes	GR, FS, H, CC, CKD, RTR, GF, CAPD	Yes	Yes, 129
10	M	No	No	GR, FS, H, CC, CKD	No	Expired, 8
10	M	No	No	GR, FS, CC, CKD, RTR	No	No, 3
11	M	No	Yes	GR, FS, CC, CKD, RTR	Yes	Yes, 129
10	M	No	No	GR, FS, CC, CKD	Yes	Yes, 122
6	M	Yes	Yes	GR, FS, H, CC, CKD	Yes	Expired, 30
7	M	Yes	Yes	GR, FS, H, CC, CKD	Yes	Expired, 22
8	F	Yes	Yes	GR, FS, H, CC, CKD	No	Expired, 15
1	M	Yes	Yes	GR, FS, H, CC	Yes	Yes, 122
10	M	Yes	Yes	GR, FS, H, CC, CKD	Yes	Expired, 24
2	M	Yes	Yes	GR, FS, H, CC, CKD	Yes	Expired, 4
4	F	Yes	Yes	GR, FS, H, CC, CKD	Yes	Expired, 24
12	M	Yes	No	GR, FS, H, CC, CKD	Yes	Yes, 112
20	F	No	No	GR, FS, CC, CKD, RTR, GF	No	Yes, 104
2	M	No	Yes	GR, FS, H, CC, CKD	No	Expired, 3
3	M	No	No	GR, FS, CC, CKD	Yes	Yes, 98
5	M	No	No	GR, FS, H, CC, CKD	No	Yes, 97
2	F	No	No	GR, FS, CC	Yes	Yes, 95
5	F	No	No	GR, FS, H, CC, CKD	No	Expired, 3
3	F	No	No	GR, FS , CC	No	Expired, 3
5	M	Yes	No	GR, FS, CC, CKD	No	Expired, 36
6	M	Yes	No	H, CC, CKD, CAPD	Yes	Yes, 82
2	F	Yes	No	GR, CC	Yes	Yes, 82
3	M	Yes	No	GR, FS, H, CC, CKD	Yes	Yes, 72
6	M	Yes	No	CKD, RTR	Yes	Yes, 65
3	M	No	No	GR, FS, H, CC	No	Yes, 44
7	M	No	No	H, CC, CKD	No	No, 42
5	F	No	No	GR, FS, CC, CKD	No	Yes, 34
21	M	No	Yes	GR, CC, CKD, RTR	Yes	Yes, 21
8	M	No	Yes	GR, H, CC, CKD	No	Expired, 12
16	M	No	No	FS, H, CC, CKD	No	Yes, 15
1	M	No	Yes	GR, FS, CKD	Yes	Yes, 13
3	F	No	No	GR, FS, CC, CKD	No	Yes, 13
9	M	No	No	GR, FS, H, CC, CKD	Yes	Yes, 6
6	M	No	Yes	GR, FS, H, CC, CKD	Yes	Yes, 6
3	M	No	Yes	GR, FS	Yes	Yes, 6
3	F	No	No	GR, FS, CC	Yes	Yes, 5
13	F	No	No	GR, FS, CC, CKD	Yes	Yes, 4
2	F	No	No	GR, CC, CKD	No	Yes, 3
3	F	No	No	GR, FS, CC, CKD	Yes	Yes, 2
1	M	No	No	GR, FS	No	Yes, 1

M=Male, F=Female, GR=Growth retardation, FS=Fanconi syndrome, H=Hypothyroidism, CC=Corneal crystals, CKD=Chronic kidney disease, RTR=Renal transplant recipient, GF=Graft failure, CAPD=Continuous ambulatory peritoneal dialysis

Conflicts of interest

There are no conflicts of interest.

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References

1. Bäumner S, Weber LT. Nephropathic cystinosis: Symptoms, treatment, and perspectives of a systemic disease. Front Pediatr 2018;6:58.
2. Tang S, Danda S, Zoleikhaeian M, Simon M, Huang T. An Indian boy with nephropathic cystinosis: A case report and molecular analysis of CTNS mutation. Genet Test Mol Biomarkers 2009;13:435-8.
3. Raut S, Khandelwal P, Sinha A, Thakur R, Puraswani M, Velpandian T, *et al*. Infantile nephropathic cystinosis: Clinical features and outcome. Asian J Pediatr Nephrol 2020;3:15-20.
4. Ravichandran R. Cystinosis: A truly orphan disease. Report of the cystinosis foundation India. Rare Dis Orphan Drugs 2016;3:1-4.
5. Bertholet-Thomas A, Berthiller J, Tasic V, Kassai B, Otukesh H, Greco M, *et al*. Worldwide view of nephropathic cystinosis: Results from a survey from 30 countries. BMC Nephrol 2017;18:210.

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